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A mathematical model with numerical simulations for malaria transmission dynamics with differential susceptibility and partial immunity

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ABSTRACT

Malaria is a deadly vector-borne infectious disease with high prevalence in the world's endemic tropical and subtropical regions. Differences in individuals' disease susceptibility may lead to their differentiation of susceptibility to infection. We formulate a mathematical model for malaria transmission dynamics that accounts for the host's differential susceptibility, where partial immunity is acquired after infection. As customary, the explicit formula for the basic reproduction number is derived and used to determine the local stability of the model's equilibria. An analysis of a special case with two susceptible classes shows that the model could have two endemic equilibria when the disease threshold parameter is less than unity. Numerical simulations are provided for a differential susceptibility when individuals are re-infected seven times after the initial infection. Graphical representations show that the transient transmission dynamics of the infected components are indistinguishable when there is no inflow into the susceptible classes. When there is an inflow into the various susceptible classes, the graphs of the infected component of the model are fundamentally different, showing that individuals who have been infected multiple times tend to be less infected over time. Knowledge of the inflow rate and the infection reduction rate due to prior infection in each class could be key drivers to mitigate the burden of malaria in a community.

1. Introduction

Vector-borne disease epidemics are a serious global threat [1]. Malaria, one of the longest-known and deadliest parasitic infectious diseases transmitted via the bite of infected adult female Anopheles mosquitoes has been plaguing mankind for centuries [2]. Globally, there were an estimated 241 million malaria cases and 627 000 malaria deaths in 85 malaria endemic countries in 2020, representing about 14 million more cases and 69 000 more deaths compared to 2019 [3]. Approximately two-thirds of these additional deaths (47 000) were linked to disruptions in the provision of malaria prevention, diagnosis, and treatment due the Covid-19 pandemic [3]. Geographic conditions, population characteristics, demographic factors such as age, gender, ethnicity, and occupation contribute to malaria transmission [4]. The high prevalence of malaria in endemic areas (tropical and subtropical regions of the world) generally stems from recurrence events, often associated with repeated infections [5,6]. While repeated exposure to an infectious agent that causes mortality and morbidity is a major health issue, it has however been reported that both naturally acquired and vaccine-induced immunity to malaria tend to be short-lived in the absence of parasite exposure [7]. In fact, individuals living in malaria hyper- or holo-endemic areas acquire natural immunity through repeated exposures that contribute to the inefficient acquisition and relatively rapid loss of the parasite [8], and the slow development of specific, acquired immunity to asexual blood stage parasites [9–12]. Thus, from the aforementioned, individuals in the community can be categorized into several states in which those with previous malaria infection can be re-infected with the disease, but they could have gradually developed some partial immunity [13]. It is therefore important to study the resulting population level effect due to the differences in individuals' disease susceptibility. For more than a century, mathematical models have been used to provide a framework for understanding malaria transmission dynamics, see [14] and the references therein.

Variation of susceptible individuals, possibly caused by genetic factors, age, health, vaccination, or past exposure to the disease, may

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lead to their differentiation of susceptibility to infection [2,15,16]. Heterogeneity in individual's susceptibility is a key determinant of infectious disease dynamics, but it is often not taken into consideration in assessing disease control measures [17]. Heterogeneity in human societies influence virus transmission [18]. Therefore, understanding how differential susceptibility could impact disease dynamics in a population, and how control measures could change this distribution, is important to predicting the dynamics of a disease. Susceptibility is assumed to change/decrease with repeated infections. How to approximate the time-varying population susceptibility has been described in [1], while immunization through vaccination has been the cornerstone of public health policy [19], most vaccine are only partially effective (that is they are not perfect), and consequently, vaccinated individuals may still contract the disease (though they may only experience mild symptoms) [20,21]. This is often the case if the virus produces mutants (vaccine escape mutants) that are not recognized by the antibodies to prevent them from eliminating the invaders [15]. As a result, vaccinated individuals may still be differentially susceptible to the infection. This is the situation with the ongoing Covid-19 pandemic which has seen many fully vaccinated and boosted individuals getting infected, though often with a different strain of the disease [20]. Rubella is another disease that needs two doses of live-attenuated vaccines to be administered for prevention [22]. Because the susceptibility varies from individual to individual, differential susceptibility to an infection can occur after vaccination is administered for some infectious diseases [21].

The susceptibility of individuals may vary during their life time, which could be due to the development of the immune system or through immunization [23]. Individuals' susceptibility to a particular infection drops to virtually near zero level for a long time after successful and completed vaccination, though for some diseases like Pertussis, the immunity acquired via vaccination can wane after some time leading to a rise in the susceptibility [24], or immunity failure after measles vaccination, despite the very reliable measles vaccine [25]. These make mathematical models' susceptibility-dependence particularly relevant for health policy and decision makers.

While some studies have considered differential infectivity in diseases such as HIV, in the staged progression case, the infected individuals sequentially pass through a series of stages, while in the differential infectivity hypothesis, infected individuals enter one of several groups, depending on their infectivity [15,26–28]. That is, for differential infectivity model, the infected population is subdivided into say n subgroups $I_1, I_2, \ldots, I_n$, and upon infection, an individual enters subgroup i and stays in that group until becoming inactive in transmission. For the staged progression model, there are multiple infection stages such that infected susceptible individuals enter the first subgroup I_1, and individuals in I_1 progress to I_2, … [29,30]. Afshar and Razvan [31] showed that using a differential infectivity model can help to mitigate the costs of the epidemic spreading. Ponnudurai et al. [32] investigated a differential infectivity of Plasmodium for the mosquito population. Malaria model with variable attractiveness have also been studied and the authors concluded that personal protection fails with increasing degree of attractiveness [33]. Since the impact of differential infectivity has been investigated in [15,27,28], herein, we shall focus on assessing the potential impact of differential susceptibility to malaria transmission dynamics.

Some studies have investigated the potential impact of individuals' differential susceptibility to disease dynamics [31,34,35]. Differential susceptibility typically means heterogeneity in the susceptible population, but here, it is specifically referring to changes in susceptibility due to repeated infections. Li et al. [34] conducted a theoretical study of a vector-borne disease model with direct transmission and age-structured differential susceptibility in the host population. As disease process is different in male or female, children or adult, … [31], with susceptibility dependent on genetic, physiological, or social characteristics that vary between individuals, Hincapie and Ospina [35] investigated the potential impact of differential susceptibility in a malaria model with control measures, namely: insecticide-treated nets and educational campaigns. It is important to note that susceptibility is assumed to change with repeated infections, that is parameters indexed by i such as the death rate would decrease due to partial immunity, but by how much or how exactly, is a question for future investigation. Because of this unknown, specific values for some of the model parameters are not provided, but for illustration purpose, a range of parameter values are given.

The effects of variation in susceptibility to measles, smallpox, and whooping cough have been studied by simply including periodic variations in susceptibility, but with a single equation for the susceptible individuals. Periodic variations make the models time-dependent and mathematically intractable. Because variation of susceptible individuals could be due to age, health, vaccination, or past exposure to the disease, our proposed model builds on previous studies and extends them as follows—Li [13] investigated a malaria model with partial immunity in humans by constructing a compartmental model with several susceptible classes, but with inflow only in the first susceptible subgroup. Ducrot et al. [27] considered two host types in the human population, the *non-immune* comprising all humans who have never acquired immunity against malaria and the *semi-immune*, and obtained an explicit expression of the reproduction number as a function of the weight of the transmission *semi-immune-mosquito-semi-immune*, and the weight of the transmission *non-immune-mosquito-non-immune*. In [15], the authors formulated compartmental differential susceptibility models by dividing the susceptible population into multiple subgroups according to the susceptibility of individuals in each group, with one single infective class. This paper addresses an interesting question of how differences in host susceptibility due to repeated infection affects malaria dynamics. The proposed model considers both differential susceptibility and infectivity, which is the first of its kind to extend the differential susceptibility and infectivity to more than two classes, to the best of our knowledge. Individuals coming into the population can be classified into one of the susceptible subgroups as in [15], therefore, there is inflow into all the n-susceptible classes in our proposed model. Infected individuals from each susceptible class move to a corresponding infective class. Considering the two cases with and without inflow of individuals into the various susceptible classes enables us to assess the potential impact of differential susceptibility of malaria transmission transient dynamics when the disease threshold $\mathcal{R}_0 < 1$ or $\mathcal{R}_0 > 1$.

The rest of this paper is organized as follows. Section 2 introduces our proposed mathematical model of malaria with differential susceptibility. Analysis of the model is provided in Section 3, while numerical simulations are provided in Section 4. The last Section 5 concludes the paper.

2. Model description

The model consists of two populations, namely, the human and mosquito population. For simplicity and mathematical tractability, we ignore the incubating classes (exposed) and sub-divide the human population into groups of susceptible, infectives, and recovered individuals, and the mosquito population into groups of susceptible and infectives.

The total human population $N(t)$ at any given time t is stratified into mutually exclusive compartments. Using superscript h for the human host, at any time t, we let S_1^h denote the number of susceptible people who have never been infected and, $S_i^h, i = 2, \ldots, n$ the number of people who are susceptible and have been infected i-times prior to time t, I_i^h the number of infectious individuals who have also been infected i-times prior to t. For this proposed epidemic model, a susceptible individual is first infected and enters the infectious class I_1^h. After recovery, the person becomes susceptible again with partial immunity (different susceptibility) and enters into group S_2^h. When the individual recovers from the second infection, he/she becomes susceptible again

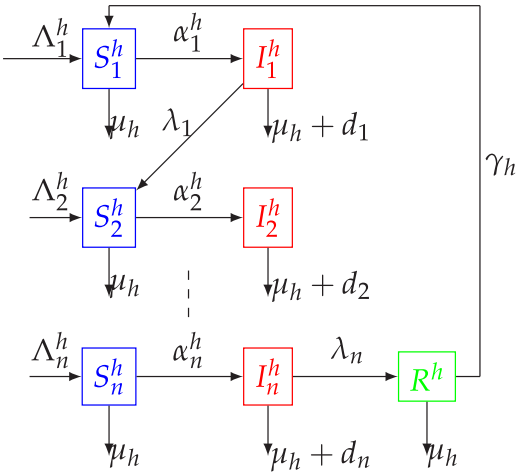


Fig. 1. Human compartmental of the model.

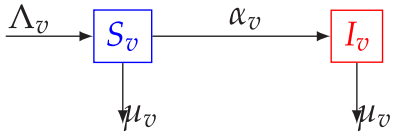


Fig. 2. Mosquitoes compartmental of the model.

Table 1
Description of the model variables.

Variable	Description
Humans	
S_i^h	Number of individuals likely to get infected for the ith time
I_i^h	Number of individuals infected for the ith time
R_h	Number of immune individuals in the population
Mosquitoes	
S_v	Number of susceptible mosquitoes
I_v	Number of infectious mosquitoes

Table 2
Model parameters.

Parameter	Description	Value	Reference
Human			
Λ_i^h	Recruitment rate in the ith susceptible	$[0, 100]$	Assumed
γ_h	Trans. rate of lost of immunity in the host pop.	0.0146	[37]
λ_i	Rate of recovery in the ith host pop.	0.0035	[37]
μ_h	Death rate for humans	$\frac{1}{55\times 365}$	Assumed
d_i	Disease-induced death rate after the ith infection	$[10^{-5}, 10^{-3}]$	[38]
a	Number of bites on humans by a one female mosquito per day	$[0.5, 5]$	
m_i	Inf. coefficient of humans likely to get infected for the ith time	$[0.016, 0.022]$	[39]
Mosquitoes			
Λ_v	Recruitment rate of mosquitoes	400	[13]
μ_v	Death rate for mosquitoes	0.033	[37]
c_i	Inf. coefficient of vector due to bite of infectious host I_i^h	$[0.42, 0.48]$	[39]
$\tilde{c}$	Inf. coefficient of vector due to bite of removed host group	0.048	[39]

Table 3
Derived model parameters.

Parameter	Formula	Description
α_i^h	$a\frac{m_i I_v}{N^h}$	Incidence rate of susceptible humans likely to get infected for the ith time
α_v	$a\frac{\tilde{c}R^h + \sum_{i=1}^{n} c_i I_i^h}{N^h}$	Incidence rate of susceptible mosquitoes

but with more immunity and reduced susceptibility. Gradually, this person moves to the final group S_n^h with (near) complete immunity. Despite the multiple challenges to understanding immunity to Plasmodium parasites and identifying the correlates of immune protection [36], the compartment R^h represents individuals who have acquire immunity and can no longer be infected by plasmodium (at least for sometime). The process of acquisition of immunity is progressive and increases over the course of repeated exposures/infections as reported in the literature [12], reason why we did not consider the classes R_i^h (for $i = 1, \ldots, n$) because after the first infection, there is certainly a small premunition which leads to a slightly different class from the completely naive susceptible S_1^h, but this small premunition cannot yet prevent one from being infected with malaria, as our interest is in the real partially immune class. That is the main reason why infected individuals in the I_1^h class fall into the S_2^h upon recovery, and so on. Thus, the R_i^h are individuals who have had repeated exposures and in the process have accumulated some temporary immunity.

The constant parameter Λ_1^h is the inflow of the susceptible people due to birth or immigration into the S_1^h-class, and Λ_i^h is the inflow of the susceptible people due to immigration into the S_i^h- class. The natural death rate is μ_h, and d_i is the malaria-induced death rate for people having been infected i-times. The parameter λ_i represents the recovery rate in the ith-class. The derived parameters α_i^h and α_v are respectively the incidence rates (forces of infection) from an infectious mosquito to a susceptible human likely to get infected for the ith-time, and the incidence rate of susceptible mosquitoes.

To account for the transmission dynamics between the mosquito and human populations, we divide the mosquito population into groups of susceptible and infective mosquitoes. Using the subscript v for vector, S_v and I_v denote the number of susceptible and infective mosquitoes, respectively. Since the lifespan of mosquitoes is shorter than their infective period, we assume that mosquitoes are neither immune nor can recover.

The model diagrams depicting flows respectively between the human and mosquitoes' classes are illustrated in Figs. 1 and 2, while all the model variables and parameters are respectively defined in Tables 1 and 2.

The case where there is no inflow to the susceptible population will assume all susceptibles are in group 1. What happens when there is no inflow but there is an initial condition with susceptibles in each group is a subject of future investigation, as this could apply to a population with little migration in/out, but that has previously been exposed to the disease.

Based on the model description and assumptions, we establish the following system of non-linear ordinary differential equations (1) (see Table 3).

$$\begin{cases} {S_1^h}' = \Lambda_1^h + \gamma_h R^h - (\alpha_1^h + \mu_h)S_1^h, \\ {S_i^h}' = \Lambda_i^h + \lambda_h I_{i-1}^h - (\alpha_i^h + \mu_h)S_i^h, \quad 2 \le i \le n, \\ {I_i^h}' = \alpha_i^h S_i^h - (\lambda_i + \mu_h + d_i)I_i^h, \quad 1 \le i \le n, \\ {R^h}' = \lambda_n I_n^h - (\gamma_h + \mu_h)R^h, \\ S_v' = \Lambda_v - (\alpha_v + \mu_v)S_v, \\ I_v' = \alpha_v S_v - \mu_v I_v. \end{cases} \tag{1}$$

with the following initial conditions

$$S_i(t) \geq 0,\ I_i(t) \geq 0,\ 1 \leq i \leq n,\quad R(t) \geq 0,\ S_v(t) \geq 0,\ I_v(t) \geq 0. \tag{2}$$

3. Model analysis

In this section, we presents a qualitative study of the dynamic properties of the model (1). The model is biologically relevant if $\forall t \geq 0$, all model variables are positive. Under the initial condition (2), the solutions of the model (1) are positive for all time $t > 0$. The feasible region of the model system (1) is given by

$$\Omega = \left\{ \left(S_1^h, \ldots, S_n^h, I_1^h, \ldots I_n^h, R^h, S_v, I_v\right) \in \mathbb{R}^{2n+3} : N_h \leq \frac{\Pi_h}{\mu_h}, N_v \leq \frac{\Lambda_v}{\mu_v} \right\},$$

with $\Pi_h = \sum_{i=1}^{n} \Lambda_i^h$.

3.1. Local stability of disease-free equilibrium

The disease-free equilibrium (DFE) is obtained by setting the right-hand side of the equations in the model (1) to zero with $I_i^h = 0$, for $1 \leq i \leq n$, $R^h = 0$ and $I_v = 0$. The system (1) admits a trivial equilibrium or (DFE) given by

$$\mathcal{E}_0 = \left(\frac{\Lambda_1^h}{\mu_h}, \frac{\Lambda_2^h}{\mu_h}, \ldots, \frac{\Lambda_n^h}{\mu_h}, \underbrace{0, \ldots, 0}_{(n+1)times}, \frac{\Lambda_v}{\mu_v}, 0 \right). \tag{3}$$

To compute the basic reproduction number $\mathcal{R}_0$, we use the next generation matrix operator [40], which consists in determining the matrix F and V and determining the spectral radius of the matrix FV^{-1}. For this, we assemble the compartments of the infected individuals from the system (1), and decompose the right hand-side as $\mathcal{F} - \mathcal{V}$, where $\mathcal{F}$ is the transmission part, expressing the production of new infected/infectious, and $\mathcal{V}$ the transition part, which describes the change in state.

$$\mathcal{F} = \begin{bmatrix} \frac{am_1 I_v}{N_h} S_1^h \\ \frac{am_2 I_v}{N_h} S_2^h \\ \vdots \\ \frac{am_n I_v}{N^h} S_n^h \\ 0 \\ a\left(\frac{\sum_{i=1}^{n} c_i I_h^i}{N^h} + \frac{\tilde{c} R^h}{N^h} \right) S_v \end{bmatrix} \quad \text{and} \quad \mathcal{V} = \begin{bmatrix} (\lambda_1 + \mu_h + d_1) I_h^1 \\ (\lambda_2 + \mu_h + d_2) I_h^2 \\ \vdots \\ (\lambda_n + \mu_h + d_n) I_h^n \\ -\lambda_n I_n^h + (\gamma_h + \mu_h) R^h \\ \mu_v I_v \end{bmatrix}.$$

Next, we calculate the Jacobian of $\mathcal{F}$ and $\mathcal{V}$ at DFE $\mathcal{E}_0$

$$F = \frac{\partial \mathcal{F}}{\partial X} = \begin{bmatrix} 0 & 0 & \ldots & 0 & 0 & \frac{am_1}{N^{h*}} S_1^{h*} \\ 0 & 0 & \ldots & 0 & 0 & \frac{am_1}{N^{h*}} S_2^{h*} \\ \vdots & \vdots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & \ldots & 0 & 0 & \frac{am_1}{N^{h*}} S_n^{h*} \\ 0 & 0 & \ldots & 0 & 0 & 0 \\ \frac{ac_1}{N^{h*}} S_v^* & \frac{ac_2}{N^{h*}} S_v^* & \ldots & \frac{ac_n}{N^{h*}} S_v^* & \frac{a\tilde{c}}{N^{h*}} S_v^* & 0 \end{bmatrix},$$

$$V = \frac{\partial \mathcal{V}}{\partial X} = \begin{bmatrix} (\lambda_1 + \mu_h + d_1) & 0 & 0 & 0 & 0 \\ \vdots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & (\lambda_n + \mu_h + d_n) & 0 & 0 \\ 0 & \ddots & -\lambda_n & (\gamma_h + \mu_h) & 0 \\ 0 & \ldots & 0 & 0 & \mu_v \end{bmatrix}.$$

The basic reproduction, unarguably one of the most important quantity in infectious disease epidemiology [41,42], is given by $\mathcal{R}_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the next-generation matrix (FV^{-1}). Thus, after some algebraic manipulations, the basic reproduction number of the model system (1) is given by

$$\mathcal{R}_0 = \sqrt{\frac{a^2 \Lambda_v \mu_h}{\Pi_h^2 \mu_v^2} \left[\sum_{i=1}^{n} \frac{m_i c_i \Lambda_h^i}{(\lambda_i + \mu_h + d_i)} + \frac{m_n \tilde{c} \lambda_n \Lambda_h^n}{(\lambda_n + \mu_h + d_n)(\gamma_h + \mu_h)} \right]}.$$

Note that the square root of the reproduction number for the entire human–mosquito populations that takes care of the scalar matching for the model [13] is the square root of the product of the two reproduction numbers. That is, the square root represents the geometric mean that takes the average number of secondary host (or vector) infections produced by a single infected host (or vector) [43].

Also, with differential susceptibility without recruitment into the first $n-1$ classes ($\Lambda_i = 0,\ 1 \leq i \leq n-1$), the expression of the threshold parameter $\mathcal{R}_0$ is the same as that of the model without differential susceptibility (i.e the $SIRS$-type model for malaria) . However, with population mobility, it is expected that recruitment into the different susceptibility classes will occur, and consequently $\Lambda_i \neq 0$ in malaria endemic communities. Hence, recruitment into the different susceptibility classes has an impact on the value of $\mathcal{R}_0$ as this could to some extent minimally increase initial disease transmission. As noted by Li [13], because the reproduction number only accounts for the initial growth of infection, it therefore characterizes the epidemic threshold under which the number of infected individuals will either increase or decrease as a small number of infectives introduced into a fully susceptible population.

3.2. Endemic equilibrium

Let $\left(S_1^{h\star}, \ldots, S_n^{h\star}, I_1^{h\star}, \ldots, I_n^{h\star}, R^{h\star}, S_v^\star, I_v^\star\right)$ be the solution of the following system of equations. We find the endemic equilibrium for the specific case of no disease-induced death rate.

$$\begin{cases} \Lambda_1^h + \gamma_h R^{h\star} - (\alpha_1^{h\star} + \mu_h) S_1^{h\star} = 0, \\ \Lambda_i^h + \lambda_i I_{i-1}^h - (\alpha_i^{h\star} + \mu_h) S_i^{h\star} = 0, \quad 2 \leq i \leq n, \\ \alpha_i^{h\star} S_i^{h\star} - (\lambda_i + \mu_h) I_i^{h\star} = 0, \quad 1 \leq i \leq n, \\ \lambda_n I_n^{h\star} - (\gamma_h + \mu_h) R^{h\star} = 0, \\ \Lambda_v - (\alpha_v^\star + \mu_v) S_v^\star = 0, \\ \alpha_v^\star S_v^\star - \mu_v I_v^\star = 0. \end{cases} \tag{4}$$

Let

$$g_i = \lambda_i + \mu_h,\ K_i = \alpha_i^h + \mu_h,\ 1 \leq i \leq n, \quad \text{and}$$

$$\varpi = K_1^\star - \frac{\lambda_n \gamma_h \alpha_n^\star}{\gamma_h + \mu_h} \left[\frac{1}{g_n K_n^\star} \Lambda_k^h + \sum_{i=2}^{n-1} \frac{\prod_{j=i}^{n-1} \alpha_j^{h\star} \lambda_j}{\Pi_{j=i}^{n} g_j K_j^\star} \Lambda_i + \frac{\Pi_{i=1}^{n-1} \alpha_i^{h\star} \lambda_i}{g_1 \Pi_{i=2}^{n} g_i K_i^\star} \right].$$

$$S_h^{1\star} = \frac{g_1\mu_h N_h^\star(\alpha_v^\star+\mu_v)\left[\Lambda_1^h N_h^\star g_2\mu_h\mu_v(\gamma_h+\mu_h)(\alpha_v^\star+\mu_v)+a\alpha_v^\star m_2(\Lambda_1 g_2(\gamma_h+\mu_h)+\Lambda_2^h\lambda_2\gamma_h m_2)\right]}{(\Lambda_2^h)^2a^2\alpha_v^{\star 2}m_1m_2\Theta+N_h^\star g_1g_2\mu_h\mu_v(\gamma_h+\mu_h)(\alpha_v^\star+\mu_v)\left[a\Lambda_v\alpha_v^\star(m_1+m_2)+N_h^\star+\mu_h\mu_v(\alpha_v^\star+\mu_v)\right]}, \tag{6}$$

Box I.

Then,

$$\begin{aligned}
&S_1^{h\star}=\frac{\Lambda_1^h}{\varpi},\quad S_v^\star=\frac{\Lambda_v}{\alpha_v^\star+\mu_v},\quad I_v^\star=\frac{\alpha_v^\star S_v^\star}{\mu_v},\\
&N_h^\star=\frac{\sum_{i=1}^n\Lambda_i}{\mu_h},\quad \alpha_i^{h\star}=am_i\frac{I_v^\star}{N_h^\star},\quad 1\le i\le n,\quad K_i^\star=\alpha_i^{h\star}+\mu_h,\\
&2\le i\le n,\\
&I_2^{h\star}=\frac{\alpha_2^{h\star}}{g_2K_2^\star}+\frac{\alpha_1^{h\star}\alpha_2^{h\star}\lambda_1}{g_1g_2K_2}S_1^{h\star},\\
&I_k^{h\star}=\alpha_k^{h\star}\left[\frac{1}{g_kK_k^\star}\Lambda_k^h+\sum_{i=2}^{k-1}\frac{\prod_{j=i}^{k-1}\alpha_j^{h\star}\lambda_j}{\Pi_{j=i}^k g_jK_j^\star}\Lambda_i^h+\frac{\Pi_{i=1}^{k-1}\alpha_i^{h\star}\lambda_i}{g_1\Pi_{i=2}^k g_iK_i^\star}S_1^{h\star}\right],\\
&3\le k\le n,\\
&S_i^{h\star}=\frac{\Lambda_i+\lambda_kI_i^{h\star}}{K_i},\quad 2\le i\le n,\quad R^{h\star}=\frac{\lambda_nI_n^{h\star}}{\gamma_h+\mu_h}.
\end{aligned} \tag{5}$$

Now that all the variables are written as functions of $\alpha_v^\star$, by using all the equations of (5) and the following definition $\alpha_v^\star=\sum_{i=1}^n\frac{am_iI_i}{N_h^\star}$, we can derive an explicit value of $\alpha_v^\star$, and consequently, the obtain endemic equilibrium.

Consider the particular case when $n=2$, we have $\varpi=K_1^\star-\frac{\lambda_2\alpha_2^{h\star}}{\gamma_h+\mu_h}\left[\frac{1}{g_2K_2^\star}\Lambda_2^h+\frac{\lambda_1\alpha_1^{h\star}}{g_1g_2K_2^\star}\right]$, and see Eq. (6) given in Box I, where $\Theta=g_1g_2(\gamma_h+\mu_h)-\lambda_1\lambda_2\gamma_h=\lambda_1\lambda_2\mu_h+\mu_h(\gamma_h+\mu_h)\left(\lambda_1+\lambda_2+\mu_h\right)$.

After some algebraic computations, we obtain $\alpha_v^\star$ as the solution of the quadratic equation

$$q_0+q_1\alpha_v^\star+q_2\alpha_v^{\star 2}=0, \tag{7}$$

with

$$q_0=\mu_v^4g_1g_2(\gamma_h+\mu_h)^2\left(1-\mathcal{R}_0^2\right)=q_0'\left(1-\mathcal{R}_0^2\right),$$

$$\begin{aligned}
q_1=\;&-a^2\Lambda_v\Lambda_1m_1\left[c_1g_2(\gamma_h+\mu_h)\left(am_2\Lambda_v+\mu_v\left(\Lambda_1^h+\Lambda_2^h\right)\right)\right.\\
&\left.+a\Lambda_v\lambda_1\lambda_2(c_r\lambda_2+c_2(\gamma_h+\mu_h))\right]\\
&-a^2\Lambda_v\Lambda_2m_2\left[g_1\left(c_2(\gamma_h+\mu_h)+c_r\lambda_2\right)\left(am_1\Lambda_v+\mu_v\left(\Lambda_1^h+\Lambda_2^h\right)\right)\right.\\
&\left.+c_1\lambda_2\gamma_hm_1m_2\right]\\
&+g_1g_2\mu_v(\gamma_h+\mu_h)\left(\Lambda_1^h+\Lambda_2^h\right)\left[a\Lambda_v\mu_v(m_1+m_2)+\Lambda_1^h+\Lambda_2^h\right],
\end{aligned}$$

$$\begin{aligned}
q_2=\;&\Lambda_v^2a^2m_1m_2\left[\lambda_1\lambda_2\mu_h+\mu_h(\gamma_h+\mu_h)\left(\lambda_1+\lambda_2+\mu_h\right)\right]\\
&+N_h^\star g_1g_2(\gamma_h+\mu_h)(a\Lambda_v(m_1+m_2)+N_h^\star\mu_h\mu_v).
\end{aligned}$$

The following result summarizes the different cases of the existence of the endemic equilibrium.

Theorem 3.1. *The model system (1) with no disease-induced death rate admits*

1. *a unique endemic equilibrium if* $\mathcal{R}_0^2>1$,
2. *a unique endemic equilibrium if* $\mathcal{R}_0^2=1$ *and* $q_1<0$,
3. *two endemic equilibria if* $1-\frac{q_1^2}{4q_2q_0'}<\mathcal{R}_0^2<1$, *and* $q_1<0$,
4. *no endemic equilibrium otherwise.*

Remark 3.1. Thus, in the case of two stages, that is when $n=2$, a backward bifurcation may occur as per the third point of Theorem 3.1.

4. Numerical simulations

Li [13] in his investigation of a malaria model with partial immunity in humans noted that while the initial infections are the same for the two cases, their endemic values and transient transmission dynamics are different. However, their study did not include inflow into the other classes. Here, we investigate the impact of inflow of individuals with different susceptibility into the other classes besides the initial susceptible class. Two scenarios are considered here (1) the case where the inflow $\Lambda_i=0,\ \forall i\neq 1$ and (2) the case where the inflow $\Lambda_i\neq 0$ for $1\le i\le 7$. In addition, because the basic reproduction number can be used to determine factors important in the ability of a disease to invade or persist [44], the figures are generated for the case $\mathcal{R}_0<1$, and $\mathcal{R}_0>1$. For illustrative purpose, seven different susceptible classes are considered, compared to only two in [13]. Our results indicates that the inflow of individuals who have gained partial immunity after repeated infections has a meaningful effect on the dynamics of malaria in a community, see Figs. 3(a) and 7(b). As expected, whether $\mathcal{R}_0$ is greater or less than one, differential susceptibility has an effect on the disease dynamics and can be seen by the reduced number of infections as the number of repeated infections increases (Figs. 6(a)–7(a)). Though the dynamics of infected mosquitoes as shown in Figs. 5(b) and 8(b) when $\mathcal{R}_0>1$ is independent of the inflow into the susceptible human classes, this is not surprising because the infected class I_v depends on the vector inflow Λ_v and not on the human inflow parameter Λ_i^h. In fact, when there is no inflow into the other susceptible classes, the figures are indistinguishable as depicted in Figs. 3(a)–5(b), while when inflow is accounted for into the classes when $2\le i\le n$ (in this case $n=7$, the effect of the repeated infections on each class is depicted in Figs. 3(a)–5(b). Consequently, the reduction of infection or the immunological memory for people who have been infected before is important. Thus, knowledge of the inflow rate as well as the infection reduction rate due to prior infection in each class could be key drivers to estimating/mitigating the burden of malaria in a community.

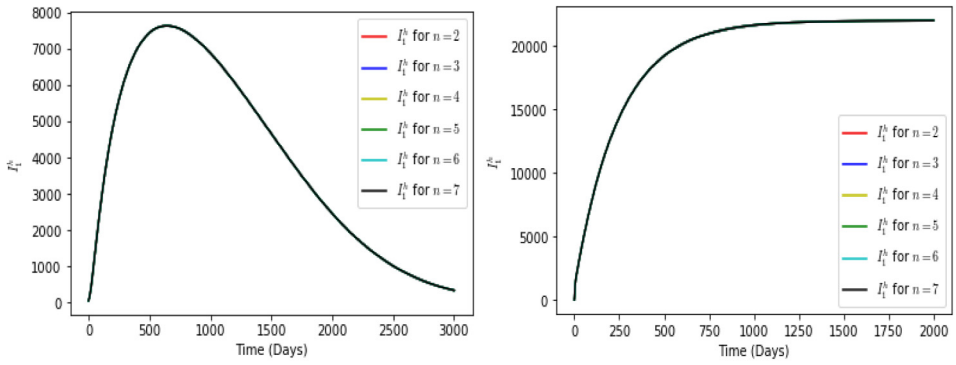
Finally, from the graphical representations depicted below, as expected, when $\mathcal{R}_0<1$, the disease can be eliminated as infections tend to the disease-free equilibrium, while for $\mathcal{R}_0>1$, the disease will persist at an endemic equilibrium. It is important to note that the inflow into the human classes and the number of human differential susceptibility classes have no effect on the mosquitoes dynamics as depicted in Figs. 5(b) and 8(b). Most importantly, differences in host susceptibility due to repeated infection affects malaria dynamics; when $\mathcal{R}_0<1$, there are fewer individuals with repeated infections (for example when $n=7$). On the other hand, when $\mathcal{R}_0>1$, the cumulative number of people with repeated malaria infections is higher. This results answers the question of how differences in host susceptibility due to repeated infection affects malaria dynamics.

4.1. Case 1: No inflow into of susceptibles into the ith-class ($\Lambda_i=0,\ \forall i\neq 1$)

See Figs. 3–5.

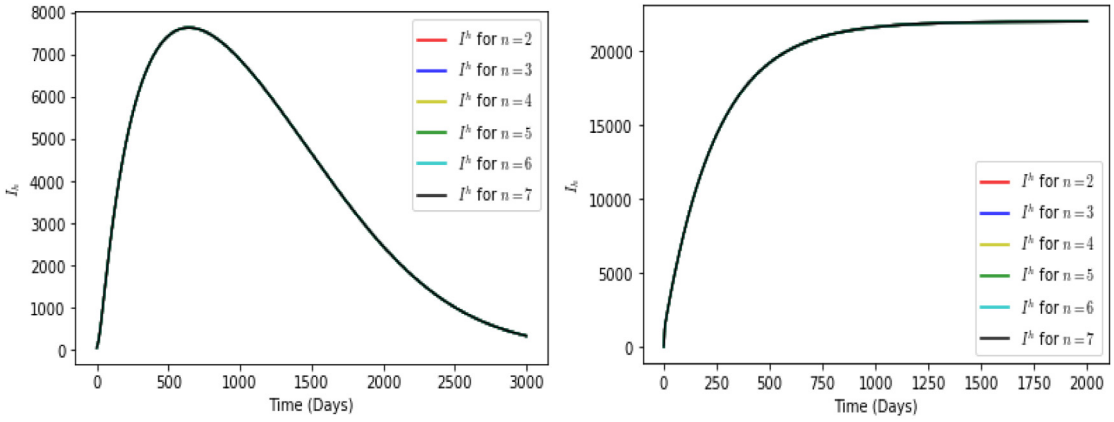
4.2. Case 2: Inflow of susceptibles into the ith-class ($\Lambda_i\neq 0$ for $1\le i\le 7$)

See Figs. 6–8.



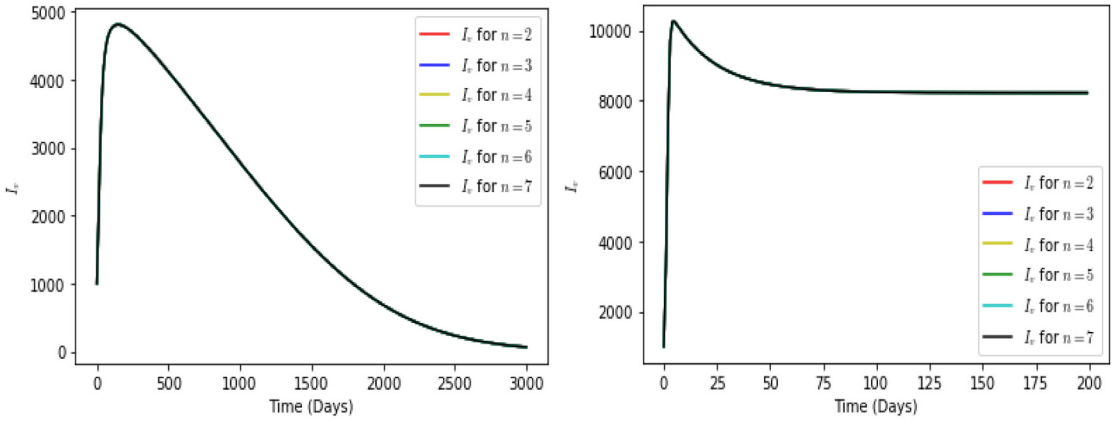
(a) Dynamic of I_1^h when $\mathcal{R}_0 = 0.2358 < 1$ (b) Dynamic of I_1^h when $\mathcal{R}_0 = 2.2470 > 1$

Fig. 3. Dynamic of the human infected classes I_j^h.



(a) Dynamic of total infectious I^h when $\mathcal{R}_0 = 0.2358 < 1$ (b) Dynamic of total infectious I^h when $\mathcal{R}_0 = 2.2470 > 1$

Fig. 4. Dynamic of total infectious I^h.

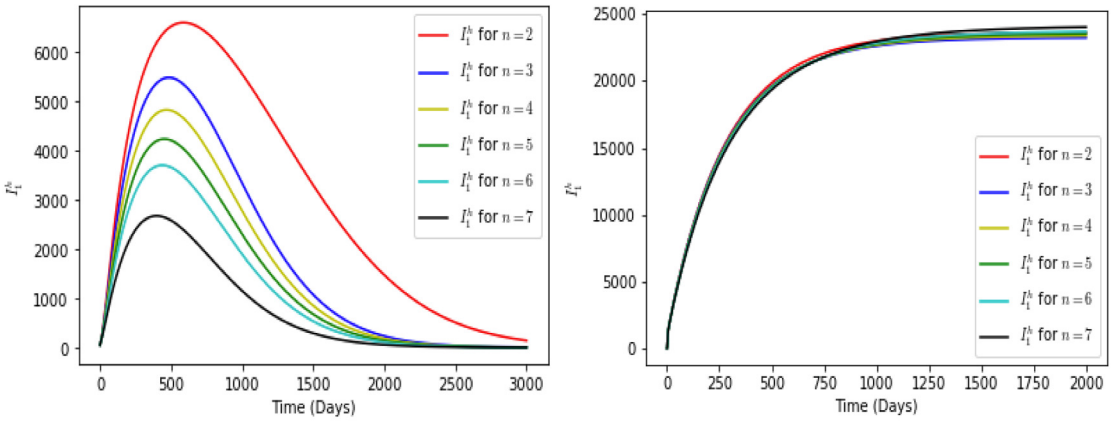


(a) Dynamic of I_v when $\mathcal{R}_0 = 0.2358 < 1$ (b) Dynamic of I_v when $\mathcal{R}_0 = 2.2470 > 1$

Fig. 5. Dynamic of the infective mosquitoes I_v.

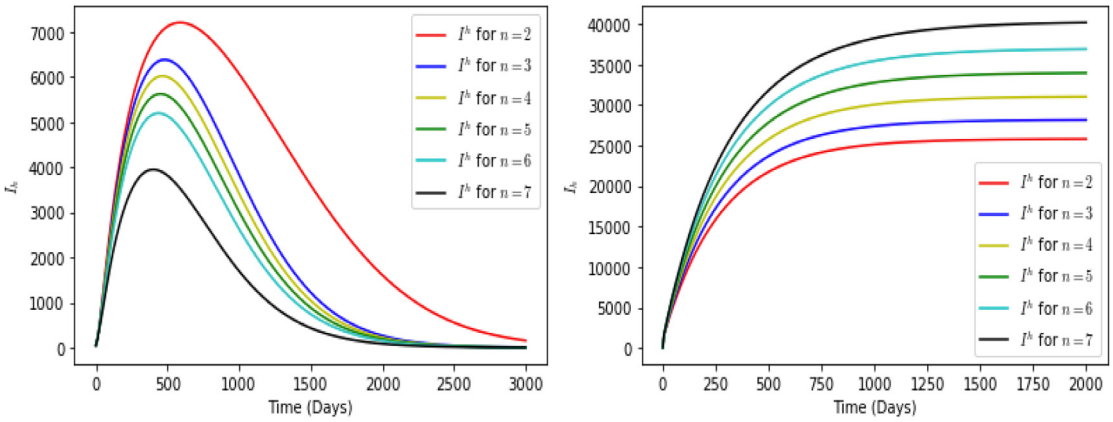
5. Conclusion

Malaria is an infectious disease and one of the leading health challenges globally, and its high prevalence in endemic areas generally stems from recurrence events [5]. After malaria treatment and recovery, a person can be re-infected. However, the mechanisms for humans acquiring partial immunity to malaria after infection though not fully understood depends on both the duration and the intensity of past exposure to infection [13]. To better understand how differential susceptibility acquired through partial immunity affects the transmission dynamics of malaria, we formulated a compartmental model, based on a system of non-linear differential equations, where the human population is sub-divided into groups according to their disease status and their susceptibility levels, with disease progression stages and partial immunity. By applying the next generation method, the model basic reproduction number is derived. The disease-free equilibrium is



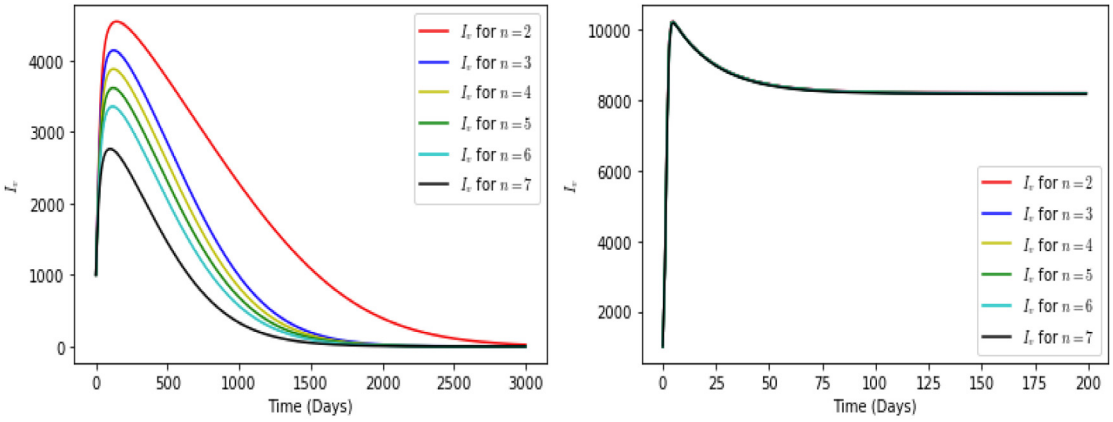
(a) Dynamic of I_1^h when $\mathcal{R}_0 = 0.2021 < 1$ (b) Dynamic of I_1^h when $\mathcal{R}_0 = 2.0241 > 1$

Fig. 6. Dynamic of I_1^h.



(a) Dynamic of total infectious I^h when $\mathcal{R}_0 = 0.2021 < 1$ (b) Dynamic of total infectious I^h when $\mathcal{R}_0 = 2.0241 > 1$

Fig. 7. Dynamic of total infectious I^h.



(a) Dynamic of I_v when $\mathcal{R}_0 = 0.2021 < 1$ (b) Dynamic of I_v when $\mathcal{R}_0 = 2.0241 > 1$

Fig. 8. Dynamic of I_v.

also derived and its local stability follows from a standard Theorem in [40]. Existence of the endemic equilibrium is investigated for the case of two stages and the model may have two endemic equilibria under certain conditions stated in Theorem 3.1.

Numerical simulations are then carried out to assess the potential impact of differential susceptibility of malaria transmission dynamics. For illustrative purpose, the simulations are conducted for a special case when $n = 7$ (that is individuals are re-infected six times after the initial infection). Results indicate that the equilibrium values when $\mathcal{R}_0 < 1$ or $\mathcal{R}_0 > 1$ and transient transmission dynamics are different for each of the infective classes. However, when there is no inflow into the susceptible classes $S_i^h, 2 \le i \le n$, the graphs of the infected component

of the model are indistinguishable. From the graphical representations, the total number of infections drops when increasing the number of infected classes with inflow to all of them, with the higher classes having decreased susceptibility.

Our modeling study has some limitations mainly due to the model structures. For mathematical convenience, we did not account for the incubating/exposed classes in both host and vector populations. Also, the multi-time scale modes could have been better due to the different vector and human lifespans. Though this could lead to infected vector being remarkably small or almost zero, the pathogen is extremely infectious and consequently, malaria prevalence in vectors is high, hence the vertical transmission. Malaria treatment resistance is also a key health issue that should be given prominence [45]. With the recent groundbreaking malaria vaccine for children below the age of five [46], a meta-population model that accounts for individuals below and above 5 years old, including differential susceptibility and infectivity is viable [47,48].

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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