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Dynamics of an age-structured two-strain model for malaria transmission

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ABSTRACT

A new age-structured deterministic model for assessing the impact of anti-malaria drugs on the transmission dynamics of malaria is designed and qualitatively analysed. The resulting two-strain age-structured model undergoes backward bifurcation, which arises due to malaria-induced mortality in humans. Conditions for the existence of unique resistant strain-only and low-endemicity equilibria are derived for special cases. It is shown, for the case when treatment does not cause drug resistance, that the disease-free equilibrium of the wild strain-only component of the model is globally-asymptotically stable whenever the associated reproduction number of the model is less than unity. Similar result is established for the resistant strain-only component of the model for this case. Numerical simulations of the model, for the case when treatment does not cause drug resistance, show that the model undergoes competitive exclusion (where the malaria strain with the higher reproduction number drives the other to extinction).

1. Introduction

Malaria, a major vector-borne disease that is endemic in over 100 countries [6,55], accounts for about 300 million cases and over one million fatalities annually (with children under the age of five suffering the most mortality burden) [55]. In addition to the public health burden it incurs, malaria also inflicts enormous socio-economic burden in malaria-endemic nations. For example, the annual economic burden of malaria in Africa alone was estimated to be around US $8 billion [6]. In the absence of an effective and safe vaccine for use against malaria in humans (although concerted global efforts are underway to develop such a vaccine [5,15,16,24,31,39–41,44,48,49,53,57,59]), malaria control is based on the use of preventive measures (such as mosquito-reduction strategies and personal protection against mosquito bite) and the use of anti-malaria drugs (see, for instance, [20,21,32,46,47,61,63]). The use of anti-malarial drugs (such as *Aralen, Chloroquine, Malaraquine and Nivaquine* [6,43]) is, however, known to pose the problem of the emergence and transmission of drug-resistant malaria strain [3,6,20,32,33,43]. Such resistance is attributed to factors such as [3,6,20,32,33,43]:

(a) Spontaneous mutations that confer reduced sensitivity to a given drug or class of drugs.
(b) Treatment failure (due to incorrect dosing, non-compliance with duration of dosing regimen, poor drug quality, drug interactions, poor or erratic absorption and misdiagnosis etc.).

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Anti-malaria drug resistance clearly poses major challenges to the global effort to effectively control the spread of malaria (or to eradicate the disease) [6,60]. Consequently, it is important to study the qualitative impact of treatment (using the currently-available anti-malaria drugs) on the transmission dynamics of malaria in a population. A number of mathematical models have been designed and used to study the transmission dynamics drug-sensitive and drug-resistant malaria in a populations (see, for instance, [3,4,11,13,20,28,33,35–38,45,56]). Probabilistic models were used in [28,36] to study the factors that influence the evolution of resistance to antimalarial drugs. Other studies, such as those in [3,11,20], employed dynamic models to assess the impact of drug treatment and resistance development on malaria transmission dynamics. A reaction–diffusion system was used in [4] to model the spatial spread of antimalarial drug resistance. The aforementioned models do not incorporate age-structure. The current study extends the aforementioned studies by designing a new age-structured model for the transmission dynamics of the drug-sensitive and drug-resistant malaria strains in a population. The paper is organized as follows. The model is formulated is Section 2 and qualitatively analysed in Section 3.

2. Model formulation

The new age-structured treatment model for malaria transmission dynamics in a community is designed by sub-dividing the total human population at time t, denoted by $N_H(t)$, into the mutually-exclusive sub-populations of susceptible juveniles ($S_J(t)$), susceptible adults ($S_A(t)$), latently-infected (asymptomatic) juveniles with the wild strain ($E_{JW}(t)$), latently-infected (asymptomatic) adults with the wild strain ($E_{AW}(t)$), latently-infected (asymptomatic) juveniles with the resistant strain ($E_{JR}(t)$), latently-infected (asymptomatic) adults with the resistant strain ($E_{AR}(t)$), symptomatic juveniles with the wild strain ($I_{JW}(t)$), symptomatic adults with the wild strain ($I_{AW}(t)$), symptomatic juveniles with the resistant strain ($I_{JR}(t)$), symptomatic adults with the resistant strain ($I_{AR}(t)$), effectively-treated juveniles ($T_J(t)$), effectively-treated adults ($T_A(t)$), recovered juveniles ($R_J(t)$) and recovered adults ($R_A(t)$), so that

$$N_H(t) = S_J(t) + S_A(t) + E_{JW}(t) + E_{AW}(t) + E_{JR}(t) + E_{AR}(t) + I_{JW}(t) + I_{AW}(t) + I_{JR}(t) + I_{AR}(t) + T_J(t) + T_A(t) + R_J(t) + R_A(t).$$

Individuals in the latently-infected classes (E_{JW}, E_{AW}, E_{JR} and E_{AR}) are asymptotically-infected (and can transmit malaria infection to susceptible mosquitoes).

The total mosquito population at time t, denoted by $N_V(t)$, is sub-divided into the compartments of susceptible mosquitoes ($S_V(t)$) and mosquitoes infected with the wild ($V_W(t)$) and resistant ($V_R(t)$) strains, so that

$$N_V(t) = S_V(t) + V_W(t) + V_R(t).$$

The population of susceptible juveniles is generated by the birth (or immigration) of juveniles (at a rate Π_J). Although vertical transmission of malaria can occur (see [19] and some of the references therein), it is assumed that all children are born susceptible (so that there is no vertical transmission of malaria from mother-to-child). This population is increased by the loss of infection-acquired immunity by recovered juveniles (at a *per capita* rate ψ_J). It is decreased by infection, following effective contacts with infected mosquitoes, at a rate λ_J, given by

$$\lambda_J = \frac{\beta_J b_1(N_V, N_H)(V_W + \theta_R V_R)}{N_V}. \tag{1}$$

In (1), β_J is the probability of infection of susceptible juveniles *per* bite by an infected mosquito and $b_1(N_V, N_H)$ is the *per capita* biting rate of mosquitoes on susceptible humans (juveniles and adults) *per* unit time. Furthermore, $\theta_R > 0$ is a modification parameter accounting for the possible variability of infectiousness of mosquitoes infected with the resistant strain (V_R) in comparison to mosquitoes infected with the wild strain. It is further decreased by maturation to adulthood (at a rate ξ; this rate is assumed to be same for all juvenile compartments. It is worth stating that although the assumption that infected juveniles can carry their infection to the next generation (to their corresponding adult classes) may not be realistic for some epidemiological settings, this study provides a robust formulation, which allows for the assessment of the cases where such an assumption is realistic or not). This population is further decreased by natural death (at a rate μ_H; it is assumed that natural death occurs in all human compartments at this rate). Thus,

$$\frac{dS_J}{dt} = \Pi_J + \psi_J R_J - \lambda_J S_J - (\xi + \mu_H) S_J. \tag{2}$$

The population of susceptible adults is generated by the maturation of susceptible juveniles (at the rate ξ) and by the loss of infection-acquired immunity by recovered adults (at a rate ψ_A). It is decreased by infection at a rate λ_A, given by

$$\lambda_A = \frac{\beta_A b_1(N_V, N_H)(V_W + \theta_R V_R)}{N_V}, \tag{3}$$

where β_A is the probability of infection of susceptible adults *per* bite by an infected mosquito. This population is further decreased by natural death. Hence,

$$\frac{dS_A}{dt} = \xi S_J + \psi_A R_A - \lambda_A S_A - \mu_H S_A. \tag{4}$$