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Modeling the Spread of Malaria

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Abstract: *Many infectious diseases including malaria are preventable, yet they remain endemic in many communities due to lack of proper, adequate and timely control policies. Strategies for controlling the spread of any infectious disease include a rapid reduction in both the infected populations (if a cure is available) as well as a rapid reduction in the susceptible class if a vaccine is available. For diseases like malaria where a vaccine has recently been developed, it therefore makes it possible to reduce the susceptible class through vaccination. In this study, we have modified the Tumwiine et al. (2007) mathematical model for the transmission of malaria by including a vaccination parameter. We have shown that the model has a unique disease-free equilibrium which is locally asymptotically stable, if* $R_o \leq 1$, *where* R_o *is a parameter which depends on the given model parameters. The analytical solution clearly shows that, with a proper combination of treatment and vaccination, malaria can be eradicated from the community.*
Keywords: *disease-free equilibrium points, Infectious disease, malaria, reproduction number, stability*

I. Introduction

Malaria, derived from male aria (Italian for "bad air") and formerly called ague or marsh fever in English, is an infectious disease. Malaria is the common name for diseases caused by single-celled parasites of the genus Plasmodium. Among the parasites of the genus *Plasmodium* four species have been identified which can cause disease in humans. These include: Plasmodium falciparum, Plasmodium vivax, Plasmodium malaria and Plasmodium ovale. Of these, Plasmodium falciparum is of greatest risk to non-immune humans. The Plasmodium falciparum variety of parasites account for 80% of cases and 90% off deaths (Kakkilaya, 2003). Children under the age of five and pregnant women are the most vulnerable to the severe forms of malaria. Each year 2-3 million children die from *Plasmodium falciparum* malaria and up to 500 million people throughout the world suffer from malaria clinical disease (Engers and Godal, 1998).

Malaria is spread by the bite of an infected female mosquito, of the genus anopheles each time the infected insect takes a blood meal. The symptoms in an infected human include bouts of fever, headache, vomiting flu-like, anemia (destroying red blood cell) and malaria can kill by clogging the capillaries that carry blood to the brain (cerebral malaria) or other vital organs. On the average the incubation period of Plasmodium falciparum is about 12 days in humans. Malaria is endemic to tropical areas where the climatic and weather conditions allow continuous breeding of the mosquito. The factors that have influenced the resurgence and spread of malaria include:

a. mosquito resistance to the usual insecticides.
b. resistance of some parasite strains to the commonly used anti malaria drugs
c. economic factors that influence the financing of malaria control operations.

The WHO revealed that most malaria high-risk areas also located in developing countries where (a) the level of education is generally low and (b) drugs can be purchased without prescriptions. A combination of (a) and (b) generally results in maladministration of the drugs.

Mosquito control is a speciality in itself and includes the use of anti-malaria vaccines, insecticides, insectidide-treated bed nets (ITNs), treatment control of breeding grounds and biological control. Each ecological region requires its own individual approach: savannah, primeval forest, agricultural areas with or without irrigation systems, the margins of uplands, desert margins and oases, city environments, coastal and marsh regions. There are many difficulties: interventions need to be maintained over large areas for very long periods of time, mosquitoes quickly become resistant to insecticides, many people will not allow their houses to be sprayed, high costs, shortage of staff, ecological collateral damage due to insecticides, political instability which interferes with long-term planning. An exclusively technical approach will not be possible without simultaneous improvement in the social and economic conditions of the population at risk.

Mathematical models play a key role in the control of malaria. Koella and Boete (2002) derived a model where humans move through multiple Susceptible Exposed-Infectious-Recovered (SEIR) stages, where a history is kept of previous infections. They include a sub model for the mosquito population with subdivisions for juveniles and adults. They used the steady state value for the adult mosquito population, from this sub model, as the input into their model for malaria transmission. They introduced dependence of the parameters for the mosquito population sub model on an environmental parameter (eg. temperature or rainfall) and calculated the dependence of the reproductive number, for the full malaria model, on this environmental parameter.

II. Role Of Mathematical Model

It is important to establish the transmission dynamics of an epidemic in order to understand and predict it. Mathematical models are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological and environmental factors on the spread of diseases. These models have played a very important role in the history and development of vector-host epidemiology.

Several authors have used mathematical models to analyze the transmission and spread of malaria. Mathematical models of malaria transmission that include both mosquito and human populations have been reviewed and discussed in detail by various authors. Nedelman (1985), did some further work on malaria model of Dietz et al. (1974), and showed that the "vaccination" rate depends on a pseudoequilibrium approximation to the differential equation describing the mosquito dynamics in the malaria model. Nedelman surveys various data sets to statistically approximate parameters such as inoculation rates, rates of recovery and loss of immunity in humans, human-biting rates of mosquitoes and infectivity and susceptibility of humans and mosquitoes. Dietz *et al*. (1974) proposed a model with two different classes of humans: one without immunity to malaria and one class with some immunity. As the non-immune class falls sick, some people recover with immunity. The immune class can get infected, but does not fall clinically ill and cannot be infectious. The model by Dietz *et al*. (1974) also included super infection, a phenomenon usually associated with macro parasites.

Yang (2000) describes a compartmental model where humans follow an SEIRS-type (with more than one immune class for humans) pattern and mosquitoes follow a Susceptible-Exposed-Infectious (SEI) pattern. Yang (2000) defines a reproductive number, R_O for this model and shows, through linear stability analysis, that the disease-free equilibrium is stable for R_O < 1. He also derived an expression for an endemic equilibrium that is biologically relevant only when R_O > 1. He used numerical simulations to support his proposition that for R_O > 1, the disease-free equilibrium is unstable and the endemic equilibrium is stable.

Castillo and Ferreira (2000) use the model by Yang (2000) to study the effects of global warming. Using the estimated increase in temperature of 1.00C − 3.50C by the year 2100, they show that it is possible in some areas of the world for R_O to increase above 1; for areas to change from a stable disease-free endemic state to one with low levels of endemicity and for other areas to change from low levels of endemicity to high levels. They, however, conclude that economic and social effects are still more important than temperature effects and a good health care system with good malaria control techniques can overcome the negative effects of an increase in temperature.

The model for malaria transmission that we modified is an extension of the equations introduced by Tunwiine *et al*. (2007). In the Tunwiine model, humans follow an SIRS-like pattern and mosquitoes follow a SI pattern, similar to that described by Yang (2000) but with only one immune class for humans. Humans move from the susceptible to the infected class at some probability when they come into contact with an infectious mosquito, as in conventional SIRS models. However, infectious people can then recover with, or without, a gain in immunity; and either return to the susceptible class, or move to the recovered class. A new feature of this model is that although individuals in the recovered class are assumed to be "immune", in the sense that they do not suffer from serious illness and do not contract clinical malaria, they still have low levels of Plasmodium in their blood stream and can pass the infection to susceptible mosquitoes. After some period of time these recovered individuals return to the susceptible class. Susceptible mosquitoes get infected and move to the infected class, at some probability when they come into contact with either infectious humans or recovered humans (albeit at a much lower probability). Both humans and mosquitoes leave the population through a density dependent natural death rate. This allows the model to account for changing human and mosquito populations. Variations in mosquito populations are crucial to the dynamics of malaria, and constant population

models do not account for this. The model also includes human disease-induced death as mortality for malaria in areas of high transmission can be high, especially in infants. In the modified model, we aim to capture some of the more important aspects of this epidemiology while still keeping it mathematically tractable. One of the major important factors that we include in the existing model is vaccination in order to determine its impact as a control measure for the spread of malaria.

2.1 DEFINITION OF TERMS

Definition 2.1.1 Susceptibles: The number of individuals who can be infected but have not yet contracted the malaria but may contract it if exposed to its mode of transmission.

Definition 2.1.2 Infected: The number of individuals who have been infected of malaria fever.

Definition 2.1.3 Recovered: The number of individuals who have recovered after treatment.

Definition 2.1.4 R_O : Basic reproduction number: The expected number of secondary cases produced by a single (typical) infection in a completely susceptible population

Definition 2.1.5 : Susceptible, Infected, Recovered

Definition 2.1.6 WHO: World Health Organization.

Definition 2.1.7 Vaccination: The introduction of a vaccine or serum into a living organism to confer immunity.

III. Parameters And Terms Of The Model

S_H (t)	the number of susceptible human host at time t
I_H (t)	the number of infected human host at time t
R_H (t)	the number of partially immune human host at time t
S_V (t)	the number of susceptible mosquito vector at time t
I_V (t)	the number of infected mosquito vectors at time t
$m = \frac{N_V}{N_H}$	the number of female mosquitoes per human host
a	the average daily biting rate on man by a single mosquito (infection rate)
b	the proportion of bites on man by a single mosquito that produce an infection
c	the probability that a mosquito becomes infectious
γ	the per capita rate of loss of immunity in human host
r	the rate at which human host acquire immunity
δ	the per capita death rate of infected human hosts due to the disease
v	the rate of recovery of human host from the disease
λ_h	the per capita natural birth rate of humans
λ_v	the per capita natural birth rate of mosquitoes
μ_h	the per capita natural death rate of humans
μ_v	the per capita natural death rate of the mosquitoes
α	the 'vaccination rate' on human

3.1 EQUATIONS OF THE MODEL

The model formulated by Tumwiine *et al*. (2007) is giving as

$$\frac{dS_H}{dt} = \lambda_h N_H - \frac{abS_H I_V}{N_H} + \nu I_H + \gamma R_H - \mu_h S_H \tag{3.1.1}$$

$$\frac{dI_H}{dt} = \frac{abS_H I_V}{N_H} - \nu I_H - rI_H - \delta I_H - \mu_h I_H \tag{3.1.2}$$

$$\frac{dR_H}{dt} = rI_H - \gamma R_H - \mu_h R_H \tag{3.1.3}$$

$$\frac{dS_V}{dt} = \lambda_v N_V - \frac{acS_V I_H}{N_H} - \mu_v S_V \tag{3.1.4}$$

$$\frac{dI_V}{dt} = \frac{acS_V I_H}{N_H} - \mu_v I_V \tag{3.1.5}$$

We assumed that all infected human who recovered are moved to the recovered class and vaccinated human have temporary immunity that expires over time and again become susceptible, hence by including a vaccination parameter, "α" the above model gives the modified model below

$$\frac{dS_H}{dt} = \lambda_h N_H - \frac{abS_H I_V}{N_H} + \gamma R_H - \mu_h S_H - \alpha S_H \tag{3.1.6}$$

$$\frac{dI_H}{dt} = \frac{abS_H I_V}{N_H} - rI_H - \delta I_H - \mu_h I_H \tag{3.1.7}$$

$$\frac{dR_H}{dt} = rI_H - \gamma R_H - \mu_h R_H + \alpha S_H \tag{3.1.8}$$

$$\frac{dS_V}{dt} = \lambda_v N_V - \frac{acS_V I_H}{N_H} - \mu_v S_V \tag{3.1.9}$$

$$\frac{dI_V}{dt} = \frac{acS_V I_H}{N_H} - \mu_v I_V \tag{3.1.10}$$

The modified model equations in proportion

We recall from the previous chapter the equations for the actual population.

$$\frac{dS_H}{dt} = \lambda_h N_H - \frac{abS_H I_V}{N_H} + \gamma R_H - \mu_h S_H - \alpha S_H \tag{3.1.6}$$

$$\frac{dI_H}{dt} = \frac{abS_H I_V}{N_H} - rI_H - \delta I_H - \mu_h I_H \tag{3.1.7}$$

$$\frac{dR_H}{dt} = rI_H - \gamma R_H - \mu_h R_H + \alpha S_H \tag{3.1.8}$$

$$\frac{dS_V}{dt} = \lambda_v N_V - \frac{acS_V I_H}{N_H} - \mu_v S_V \tag{3.1.9}$$

$$\frac{dI_V}{dt} = \frac{acS_V I_H}{N_H} - \mu_v I_V \tag{3.1.10}$$

The total population sizes N_H and N_V can be determined by $S_H + I_H + R_H = N_H$ and $S_V + I_V = N_V$ or from the differential equations

$$\frac{dN_H}{dt} = (\lambda_h - \mu_h)N_H - \delta I_H \tag{3.1.11}$$

and

$$\frac{dN_V}{dt} = (\lambda_V - \mu_V)N_V \tag{3.1.12}$$

which are derived by adding equation (3.1.6) – (3.1.8) for the human population and (3.1.9) – (3.1.10) for the mosquito vector population

In the model, the term $\frac{abS_H I_V}{N_H}$ denotes the rate at which the human hosts S_H get infected by infected mosquitoes I_V and $\frac{acS_V I_H}{N_H}$ refers to the rate at which the susceptible mosquitoes S_V are infected by infected human hosts I_H. Since it is easier to analyze our model in terms of proportions of quantities instead of actual proportions, we make the transformation $s_h = \frac{S_H}{N_H}$, $i_h = \frac{I_H}{N_H}$, $r_h = \frac{R_H}{N_H}$, $s_v = \frac{S_V}{N_V}$ and $i_v = \frac{I_V}{N_V}$ in the classes S_H, I_H, R_H, S_V and I_V in the population respectively and $m = \frac{N_V}{N_H}$. This is done by differentiating the fractions with respect to time t and simplifying as follows:

$$\begin{aligned}
\frac{ds_h}{dt} &= \frac{1}{N_H}\left[\frac{dS_H}{dt} - s_h\frac{dN_H}{dt}\right] \\
&= \lambda_h - abms_h i_v + \gamma r_h - \mu_h s_h - \alpha s_h - s_h\left[(\lambda_h - \mu_h) - \delta i_h\right] \\
&= \lambda_h - abms_h i_v + \gamma r_h - \alpha s_h - \lambda_h s_h + \delta s_h i_h \\
&= \lambda_h(1 - s_h) - abms_h i_v + \gamma r_h - \alpha s_h + \delta s_h i_h
\end{aligned} \tag{3.1.13}$$

$$\begin{aligned}
\frac{di_h}{dt} &= \frac{1}{N_H}\left[\frac{dI_H}{dt} - i_h\frac{dN_H}{dt}\right] \\
&= abms_h i_v - ri_h - \delta_h i_{h-}\mu_h i_h - i_h\left[(\lambda_h - \mu_h) - \delta i_h\right] \\
&= abms_h i_v - ri_h - \delta_h i_{h-}\lambda_h i_h + \delta i_h^2 \\
&= abms_h i_v - (r + \delta + \lambda_h)i_h + \delta i_h^2
\end{aligned} \tag{3.1.14}$$

Similarly,

$$\frac{dr_h}{dt} = ri_h - (\gamma + \lambda_h)r_h + \alpha s_h + r_h\delta i_h \tag{3.1.15}$$

$$\frac{ds_v}{dt} = \lambda_v(1 - s_v) - aci_h s_v \tag{3.1.16}$$

$$\frac{di_v}{dt} = acs_v i_h - \lambda_v i_v \tag{3.1.17}$$

subject to the restriction $s_h + i_h + r_h = 1$ and $s_v + i_v = 1$, we note that the population sizes $N_H(t)$ and $N_V(t)$ do not appear in the system. Therefore, using the relations $r_h = 1 - s_h - i_h$ and $s_v = 1 - i_v$ lead to studying the system of differential equations.

$$\frac{ds_h}{dt} = \lambda_h(1 - s_h) - abms_h i_v + \gamma(1 - s_h - i_h) - \alpha s_h + \delta s_h i_h \quad (3.1.18)$$

$$\frac{di_h}{dt} = abms_h i_v - (r + \delta + \lambda_h) i_h + \delta i_h^2 \quad (3.1.19)$$

$$\frac{di_v}{dt} = aci_h(1 - i_v) - \lambda_v i_v \quad (3.1.20)$$

in the feasible region (i.e. where the model makes biological sense)

Now we intend to analyze and investigate the existence and stability of the associated equilibrium points. Assuming that all the parameters are non-negative, and solving for the equilibrium points by setting the right-hand sides of equation (3.1.18) - (3.1.20) to zero, the system takes the form as shown:

$$\lambda_h(1 - s_h^*) - abms_h^* i_v^* + \gamma(1 - s_h^* - i_h^*) - \alpha s_h^* + \delta s_h^* i_h^* = 0 \quad (3.1.21)$$

$$abms_h^* i_v^* - (r + \delta + \lambda_h) i_h^* + \delta i_h^{*2} = 0 \quad (3.1.22)$$

$$aci_h^*(1 - i_v^*) - \lambda_v^* i_v^* = 0 \quad (3.1.23)$$

In the absence of infection, $i_v = i_h = 0$, so that equation (3.1.21) yields

$$\lambda_h - \lambda_h s_h^* + \gamma - \gamma s_h^* - \alpha s_h^* = 0$$
$$\lambda_h + \gamma = s_h^*(\lambda_h + \gamma + \alpha)$$
$$s_h^* = \frac{\lambda_h + \gamma}{\lambda_h + \gamma + \alpha}$$

Hence the model has a steady state, E_0 called the disease-free equilibrium points, where

$$E_0 = \left(\frac{\lambda_h + \gamma}{\lambda_h + \gamma + \alpha}, 0, 0\right)$$

Stability of the Disease Free Equilibrium Point

To establish the stability of this equilibrium, the Jacobian matrix of equation (3.1.21)–(3.1.23) is computed and evaluated at E_0.

Let $F_1 = \lambda_h(1 - s_h^*) - abms_h^* i_v^* + \gamma(1 - s_h^* - i_h^*) - \alpha s_h^* + \delta s_h^* i_h^*$

$F_2 = abms_h^* i_v^* - (r + \delta + \lambda_h) i_h^* + \delta i_h^{*2}$

$F_3 = aci_h^*(1 - i_v^*) - \lambda_v^* i_v^*$

$$\frac{\partial F_1}{ds_h} = -\lambda_h - abmi_v^* - \gamma - \alpha + \delta i_h^* = -(\lambda_h + abmi_v^* + \gamma + \alpha - \delta i_h^*) \qquad \frac{\partial F_1}{di_h} = -\gamma + \delta s_h^*$$

$$\frac{\partial F_1}{di_v} = -abms_h^*$$

$$\frac{\partial F_2}{ds_h} = abmi_v^* \qquad \frac{\partial F_2}{di_h} = -r-\delta-\lambda_h+2\delta i_h^* = -\left(r+\delta+\lambda_h\right)+2\delta i_h^* \qquad \frac{\partial F_2}{di_v} = abms_h^*$$

$$\frac{\partial F_3}{ds_h} = 0 \qquad \frac{\partial F_3}{di_h} = ac - aci_v^* \qquad \frac{\partial F_3}{di_v} = -aci_h^* - \lambda_v$$

At the steady states of the model, the Jacobian matrix at *E* is given by

$$J_E = \begin{bmatrix} -\left(\lambda_h + abmi_v^* + \gamma + \alpha - \delta i_h^*\right) & -\gamma + \delta s_h^* & -abms_h^* \\ abmi_v^* & -Q_T + 2\delta i_h^* & abms_h^* \\ 0 & ac\left(1-i_v^*\right) & -\lambda_v - aci_h^* \end{bmatrix} \tag{3.1.24}$$

where $Q_T = \left(r+\delta+\lambda_h\right)$

Evaluating the Jacobian in equation (3.1.24) at E_0 gives

$$J_{E_0} = \begin{bmatrix} -\left(\lambda_h+\gamma+\alpha\right) & -\gamma + \dfrac{\delta\lambda_h+\delta\gamma}{\lambda_h+\gamma+\alpha} & -abm\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right) \\ 0 & -Q_T & abm\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right) \\ 0 & ac & -\lambda_v \end{bmatrix}$$

To get the eigenvalues, we obtain the characteristic equation
Thus,

$$\left|J_{E_O} - qI\right| = \begin{vmatrix} -\left(\lambda_h+\gamma+\alpha\right)-q & -\gamma + \dfrac{\delta\lambda_h+\delta\gamma}{\lambda_h+\gamma+\alpha} & -abm\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right) \\ 0 & -Q_T-q & abm\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right) \\ 0 & ac & -\lambda_v-q \end{vmatrix} = 0$$

$$= -\left(\lambda_h+\gamma+\alpha\right)-q\begin{vmatrix} -Q_T-q & abm\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right) \\ ac & -\lambda_v-q \end{vmatrix} = 0$$

which yields

$$\left[-\left(\lambda_h+\gamma+\alpha\right)-q\right]\left[q^2+\left(Q_T+\lambda_v\right)q+Q_T\lambda_v-\frac{a^2bcm\left(\lambda_h+\gamma\right)}{\lambda_h+\gamma+\alpha}\right]=0$$

The eigenvalues of the characteristic equation are given by

$$-\left(\lambda_h+\gamma+\alpha\right),\ \frac{-\left(Q_T+\lambda_v\right)\pm\sqrt{\left(Q_T+\lambda_V\right)^2-4\left[Q_T\lambda_V-a^2bmc\left(\frac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right)\right]}}{2}$$

i.e $$-\left(\lambda_h+\gamma+\alpha\right),\ \frac{-\left(Q_T+\lambda_v\right)\pm\sqrt{\left(Q_T+\lambda_V\right)^2-4Q_T\lambda_V\left(1-R_O\right)}}{2}$$

where, $R_o=\dfrac{a^2bmc\left(\dfrac{\lambda_h+\gamma}{\lambda_h+\gamma+\alpha}\right)}{Q_T\lambda_V}$, is called the basic reproduction number.

The eigenvalues are hereby analysed

i.e $$q_1=-\left(\lambda_h+\gamma+\alpha\right)<0$$

$$q_2=\frac{-\left(Q_T+\lambda_v\right)+\sqrt{\left(Q_T+\lambda_V\right)^2-4Q_T\lambda_V\left(1-R_O\right)}}{2}$$

$$q_3=\frac{-\left(Q_T+\lambda_v\right)-\sqrt{\left(Q_T+\lambda_V\right)^2-4Q_T\lambda_V\left(1-R_O\right)}}{2}.$$

If $1-R_O>0$,

then $R_O<1$ and

$$q_2<\frac{-\left(Q_T+\lambda_V\right)}{2}+\frac{\sqrt{\left(Q_T+\lambda_V\right)^2}}{2}=0$$

and $$q_3<\frac{-\left(Q_T+\lambda_V\right)}{2}-\frac{\sqrt{\left(Q_T+\lambda_V\right)^2}}{2}=-\left(Q_T+\lambda_V\right)$$

Therefore, $q_2<0$ and $q_3<0$ thus establishing $q_1<0,\ q_2<0,\ q_3<0$

Theorem

Giving the system of equation in (3.1.21)–(3.1.23) and that $r,\delta,\lambda_h,\gamma,\lambda_v$ and $R_O<1$, then the disease-free equilibrium state is locally and asymptotically stable.

IV. Conclusion

This study modified a model of malaria formulated by Tumwiine *et al*. (2007) by including a vaccination parameter, α . Analytical study was carried out on both models using the method of linearized stability and the results showed that the disease-free equilibrium points are locally asymptotically stable for the modified model. The analytical results on the modified models revealed that eradication is possible with a combination of both treatment and vaccination as a new control strategy.

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