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Relapse Effect on the Dynamics of Malaria in Humans and Mosquitoes: A Mathematical Model Analysis

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Abstract: *In this paper we consider nonlinear dynamical system to study the dynamics of malaria with relapse effect in both human and mosquito population. The total population is divided in to six compartments in which human population into three compartments and mosquito population into two compartments. We found the dynamical system has disease free equilibrium point and endemic equilibrium point. We also found that the basic reproduction number of the considered dynamical system is* $R_0 = \sqrt{\frac{q\beta(r_2+\rho+\mu)[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}{\eta(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-\eta r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}}$ *which depends on twelve parameters. We proved that the disease-free equilibrium point is locally asymptotically stable if* $R_0 < 1$ *and the endemic equilibrium point is locally stable if* $R_0 > 1$. *We also proved that the global asymptotically stability of both equilibrium points using Lyapunov functions. Using standard data collected from different sources we found the numerical value of the basic reproduction number is* $R_0 = 1.2736$ *which shows that the malaria disease spreads in the community. We have done also sensitivity analysis to identify the most influential parameter that affects the basic reproduction number and we found that the most sensitive parameter is the human recovery rate* τ *from an infectious human to a recovered human. The analytical findings are supported by the numerical simulation of the dynamical system.*

Key words: *Dynamics of Malaria,relapse effect,basic reproduction number, stability analysis, sensitivity analysis, numerical simulation.*

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I. Introduction

Malaria is an infectious disease caused by the plasmodium parasite transmitted to humans through the bite of female Anopheles mosquito.Most malaria cases and deaths occur in Sub Saharan Africa [6].In 2016, 91 countries reported a total of 216 million cases of malaria, an increase of 5 million cases over the previous year. The global tally of malaria deaths reached 445 000 deaths, about the same number reported in 2015, most of which were in children aged under 5 years in Africa. Of the 91 countries reporting indigenous malaria cases and deaths in 2016, 15 countries all in sub-Saharan Africa, except India carried 80% of the global malaria burden[15].

Mathematical models for the transmission dynamics of malaria are useful in providing better insights into the behavior of the disease. The study on malaria using mathematical modeling began in 1911 with Ross's model.He introduced the first deterministic differential equation model of malaria by dividing the human population into susceptible S_h and infected I_h compartments with the infected class returning to susceptible class again leading to the SIS structure.The mosquito population also has only two compartments susceptible S_m and infected $I_m$but they do not recover from infection due to their short life span and thereby follow the SI structure[14].

After about forty years George Macdonald [9]in the 1950s, reasserted the usefulness of mathematical epidemiology based on twenty years of fieldwork. He modified Ross's model by integrating biological information of latency in the mosquito due to malaria parasite development. The simple Ross model did not consider this latency period of the parasite in mosquitoes and their survival during that period. Macdonald considered this latency periodτ_m and introduced the Exposed $E_m$class in the mosquitoes' structure[2, 10].

Further extension was described by Anderson and May in 1991 [1]where the latency of infection in humans was introduced by making the additional exposed compartment E_h class in humans' structure.According to a review in [10]all other models that exist for malaria dynamics are developed from the three basic models explained earlier by incorporating different factors to make them biologically more realistic in explaining disease prevalence and prediction. Epidemiological studiesin [2, 5, and 11]considered the inclusion of the recovered class which incorporates a time dependent immunity developed on recovery from infection in humans.Some models have integrated other factors such as environmental effects in the work of [16, 17]and

mosquito's resistance to insecticides and resistance of some parasite strains to anti-malaria drugs in the work of [12].In 2000 Ngwa and Shu [11]proposed set of ordinary differential equationsbased compartmental model for the spread of malaria with a susceptible-exposed-infectious-recovered-susceptible SEIRS pattern for humans and a susceptible-exposed-infectious SEI pattern for mosquitoes by introducing the 'Recovered' class in humans in Anderson-May model.

In this work we considered the work done by Hai-Feng Huo and Guang-Ming Qiu in 2014 [7]introduced a mathematical model of malaria with relapse. They proposeda more realistic mathematical model of malaria in which they did not only consider the recovered humans return to the susceptible class but also considered the recovered humans return to the infectious class. We are interested to modify this model by adding one compartment namely treatment class in the human structure because humans with incomplete treatment may not recover. In addition, we consider that relapse occurs not only because of incomplete treatment but also when symptoms reappear after the parasites had been eliminated from blood but persist as dormant hypnozoites in liver cells. This commonly occurs between 8 to 24 weeks and is commonly seen with P. vivaxand P. ovaleinfections[3].

1. The Mathematical Model

Our initial Mathematical model (1) − (5) below is a model developed by Hai-Feng Huo and Guang-Ming Qiu in 2014 [7]. They introduced a mathematical model of malaria with relapse entitled by Stability of a Mathematical Model of Malaria Transmission with Relapse. Based on their own assumptions they build a dynamical system given by

$$\frac{dS_h(t)}{dt} = \mu N - \frac{\beta S_h I_m}{N} + \rho_1 R_h - \mu S_h \quad (1)$$

$$\mathbf{\frac{dI_h(t)}{dt} = \frac{\beta S_h I_m}{N} + \rho_2 R_h - (\gamma + \mu) I_h} \quad (2)$$

$$\frac{dR_h(t)}{dt} = \gamma I_h - (\rho_1 + \rho_2 + \mu) R_h \quad (3)$$

$$\frac{dS_m(t)}{dt} = \eta M - \frac{\alpha_1 S_m I_h}{N} - \frac{\alpha_2 S_m R_h}{N} - \eta S_m \quad (4)$$

$$\frac{dI_m(t)}{dt} = \frac{\alpha_1 S_m I_h}{N} + \frac{\alpha_2 S_m R_h}{N} - \eta I_m \quad (5)$$

where $S_h, I_h, R_h, S_m, I_m, N,$ and Mrepresent the number of susceptible humans, infectious humans, recovered humans, susceptible mosquitoes, infectious mosquitoes, the total size of the human population, and the total size of the mosquito's population, respectively. μis the natural birth and death rate of humans, ηis the natural birth and death rate of mosquitoes, βis from an infectious mosquito to a susceptible human transmission rate in humans, $\alpha_1$and $\alpha_2$represent both infectious and recovered human to a susceptible mosquito transmission rate in mosquitoes, γis treatment rate, $\rho_1$is recovery rate (individuals from recovered class could back to susceptible class again because they had a very small amount of parasites, which would be cleared quickly by their own immune system), $\rho_2$is relapse rate, and qis the number of mosquitoes per individual.

We add more assumptions on their model such as: When an infectious mosquito bites a susceptible human, the parasite (in the form of sporozoites) will be passed on to the human and that the person will move to the infected/infectious classI_h, with a transmission rate in human β. An infectious human who starts treatment will move to the treatment class T_h, by the rate δ; those who complete their treatment successfully will go to recovered class, by the rate γ; and those who do not get complete and adequate treatment will return to their infectious class, by the relapse rate r_1, Also, infected individuals recover spontaneously at a rate τ to join the immune class. However, the recovered human has some immunity to the disease for some period of time and later loses the immunity to become susceptible again at a rate ρ. Another relapse occurs (from the recovered class to the infected class) when symptoms reappear after the parasites had been eliminated from blood but persist as dormant hypnozoites in liver cells, by the relapse rate r_2.When a susceptible mosquito S_m bites an infectious human or human in treatment class, the parasite (in the form of gametocytes) enters the mosquito, and the mosquito moves from the susceptible to the infectious mosquito class I_m by the rates α_1 and α_2 respectively and μ is the natural birth and death rate of humans, η is the natural birth and death rate of mosquitoes. That is, the total size of human population N and the total size of mosquito population M are constants. Based on these assumptions we construct the following flow chart which shows the dynamics of malaria in human and mosquito population.

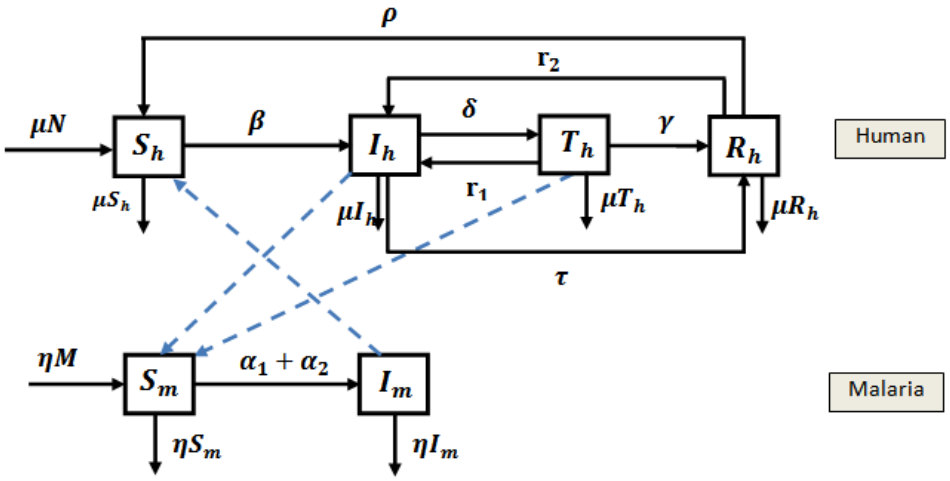

Figure 1: Transfer diagram of the model

The corresponding dynamical system of the above flow chart that we develop is

$$\frac{dS_h(t)}{dt} = \mu N - \frac{\beta S_h I_m}{N} + \rho R_h - \mu S_h \quad (6)$$

$$\frac{dI_h(t)}{dt} = \frac{\beta S_h I_m}{N} + r_1 T_h + r_2 R_h - (\delta + \tau + \mu) I_h \quad (7)$$

$$\frac{dT_h(t)}{dt} = \delta I_h - (r_1 + \gamma + \mu) T_h \quad (8)$$

$$\frac{dR_h(t)}{dt} = \gamma T_h + \tau I_h - (r_2 + \rho + \mu) R_h \quad (9)$$

$$\frac{dS_m(t)}{dt} = \eta M - \frac{\alpha_1 S_m I_h}{N} - \frac{\alpha_2 S_m R_h}{N} - \eta S_m \quad (10)$$

$$\frac{dI_m(t)}{dt} = \frac{\alpha_1 S_m I_h}{N} + \frac{\alpha_2 S_m R_h}{N} - \eta I_m \quad (11)$$

α_1	From an infectious human to a susceptible mosquito, transmission rate in mosquitoes
α_2	From a treated human to a susceptible mosquito, transmission rate in mosquitoes
β	From an infectious mosquito to a susceptible human, transmission rate in humans
N	The total size of human population
M	The total size of mosquito population
μ	Natural birth and death rate of humans
δ	Treatment rate
r_1	From a treated human to an infectious human, relapse rate
r_2	From a recovered human to an infectious human, relapse rate
γ	From a treated human to a recovered human, recovery rate
ρ	From a recovered human to a susceptible human, rate of loss of immunity
τ	From an infectious human to a recovered human, recovery rate
η	Natural birth and death rate of mosquitoes
q	The number of mosquitoes per individual

Table 1: Parameters description of the modified Mathematical model

In the modified Mathematical model$N$ and $M$are constants so by introducing new variables:

$s_h = \frac{S_h}{N}$, $i_h = \frac{I_h}{N}$, $t_h = \frac{T_h}{N}$, $r_h = \frac{R_h}{N}$, $s_m = \frac{S_m}{M}$ and $i_m = \frac{I_m}{M}$ with $s_h + i_h + t_h + r_h = 1$ and $s_m + i_m = 1$

we get an equivalent dynamical system

$$\frac{ds_h}{dt} = \mu - q\beta s_h i_m + \rho r_h - \mu s_h \quad (12)$$

$$\frac{di_h}{dt} = q\beta s_h i_m + r_1 t_h + r_2 r_h - (\delta + \tau + \mu) i_h \quad (13)$$

$$\frac{dt_h}{dt} = \delta i_h - (r_1 + \gamma + \mu) t_h \quad (14)$$

$$\frac{dr_h}{dt} = \gamma t_h + \tau i_h - (r_2 + \rho + \mu) r_h \quad (15)$$

$\frac{ds_m}{dt} = \eta - \alpha_1 s_m i_h - \alpha_2 s_m t_h - \eta s_m$ (16)

$\frac{di_m}{dt} = \alpha_1 s_m i_h + \alpha_2 s_m t_h - \eta i_m$ (17)

Positivity of Solutions

For system of differential equations (12) to (17) to ensure the solutions of the system with positive initial conditions remain positive for all $t > 0$, it is necessary to prove that all the state variables are nonnegative so we do have the following theorem

Theorem

If$s_h(0) > 0, i_h(0) > 0, t_h(0) > 0, r_h(0) > 0, s_m(0) > 0, i_m(0) > 0$thenthesolutions $s_h(t), i_h(t), t_h(t), r_h(t), s_m(t)$ and $i_m(t)$of system (12)-(17)are positive for all $t > 0$.

Proof

i. From the first equation (12) of the dynamical system we have

$\frac{ds_h}{dt} = \mu - q\beta s_h i_m + \rho r_h - \mu s_h$ whose solution is $s_h(t) = e^{-Q(t)+Q(0)}s_h(0) + \int_0^t e^{Q(s)-Q(t)}f(s)ds > 0$. Since $s_h(0) > 0$ and$f(t) > 0$ forall$t > 0$and also the exponential function always positive, then the solutions$_h(t) > 0$forall$t > 0$.

ii. From the second equation (13) of the dynamical system we have

$\frac{di_h}{dt} = q\beta s_h i_m + r_1 t_h + r_2 r_h - (\delta + \tau + \mu)i_h$ Whose solution is

$i_h(t) = e^{-kt}i_h(0) + \int_0^t e^{k(s-t)}f(s)ds > 0$. Since $i_h(0) > 0$ and$f(t) > 0$ forall $t > 0$ and also the exponential function always positive, then the solution$i_h(t) > 0$ forall $t > 0$.

iii. From the third equation (14) of the dynamical system we have

$\frac{dt_h}{dt} = \delta i_h - (r_1 + \gamma + \mu)t_h$ whose solution is $t_h(t) = e^{-kt}t_h(0) + \int_0^t e^{k(s-t)}f(s)ds > 0$.

Since $t_h(0) > 0$ and$f(t) > 0$ forall$t > 0$ and also the exponential function always positive, then the solution $t_h(t) > 0$ forall$t > 0$.

iv. From the fourth equation (15) of the dynamical system we have

$\frac{dr_h}{dt} = \gamma t_h + \tau i_h - (r_2 + \rho + \mu)r_h$whose solution is $r_h(t) = e^{-kt}r_h(0) + \int_0^t e^{k(s-t)}f(s)ds > 0$

Since $r_h(0) > 0$ and $f(t) > 0$ for all $t > 0$ and also the exponential function always positive, then the solution $r_h(t) > 0$ for all $t > 0$.

v. From the fifth equation (16) of the dynamical system we have

$\frac{ds_m}{dt} = \eta - \alpha_1 s_m i_h - \alpha_2 s_m t_h - \eta s_m$whose solution is

$s_m(t) = e^{-Q(t)+Q(0)}s_m(0) + \int_0^t e^{Q(s)-Q(t)}f(s)ds > 0$. Since

$s_m(0) > 0$ and$f(t) > 0$ forall$t > 0$ and also the exponential function always positive, then the solutions$_m(t) > 0$forall $t > 0$.

vi. From the sixth equation (17) of the dynamicalsystem we have

$\frac{di_m}{dt} = \alpha_1 s_m i_h + \alpha_2 s_m t_h - \eta i_m$whose solution is

$i_m(t) = e^{-\eta t}i_m(0) + \int_0^t e^{\eta(s-t)}f(s)ds$. Since$i_m(0) > 0$ and$f(t) > 0$ forall$t > 0$ and also the exponential function always positive, then the solution $i_m(t) > 0$ forall$t > 0$. this completes the proof of the Theorem. Therefore, the solution of the model is positive.

Boundedness of the solutions

Theorem

The feasible region of the system of differential equations (12)− (17) is given by

$\Omega = \{(s_h, i_h, t_h, r_h, s_m, i_m) \in R_+^6 \mid 0 < s_h \leq 1,\ 0 \leq i_h + t_h + r_h < 1, 0 < s_m \leq 1, 0 \leq i_m < 1\}$is positively-invariant.

Proof

From the theorem of positivity, we have seen that at the initial time $t = 0$ all the state variables are non-negative. That is, $s_h > 0$, $i_h \geq 0$, $t_h \geq 0$, $r_h \geq 0$, $s_m > 0$, and $i_m \geq 0$. From the relation of dynamical system (12) - (17) we do have $s_h + i_h + t_h + r_h = 1$ and thus $s_h = 1 - (i_h + t_h + r_h) > 0$ which implies that $i_h + t_h + r_h < 1$ and therefore $0 \leq i_h + t_h + r_h < 1$. This also implies that $s_h = 1 - (i_h + t_h + r_h) \leq 1$.Therefore $s_h \leq 1$ and hence $0 < s_h \leq 1$. Again from in the mosquito dynamics we do have $s_m + i_m = 1$ that is $s_m = 1 - i_m > 0$ which implies that $i_m < 1$ and therefore $0 \leq i_m < 1$. This also implies that $s_m = 1 - i_m \leq 1$.therefore $s_m \leq 1$ and hence $0 < s_m \leq 1$.This completes the proof of the Theorem. Therefore, the solution of the model is bounded. Furthermore, in Ω, the usual existence, uniqueness, and continuation results hold for the

system, so that the system (12)−(17), is well-posed mathematically and epidemiologically. So, we consider dynamics of system (12)−(17) on the set Ω in this paper.

II. Existence and Stability Analysis of the Equilibrium points

1.1. Disease Free Equilibrium point E_0

Disease-free equilibrium points are steady-state solutions where there is no disease. We define the "diseased" classes as the human or mosquito populations that are either infectious, treated or recovered, that are, i_h, t_h, r_h and i_m. The disease-free equilibrium of the model (12) to (17), is obtained by setting $\frac{ds_h}{dt} = \frac{di_h}{dt} = \frac{dt_h}{dt} = \frac{dr_h}{dt} = \frac{ds_m}{dt} = \frac{di_m}{dt} = 0$. Further at the disease-free equilibrium points there are neither infectious, treated nor recovered people and mosquito, that is, $i_h = 0$, $t_h = 0$, $r_h = 0$ and $i_m = 0$. Up on substituting these in equations (8) and (12),

we get $\frac{ds_h}{dt} = \mu - \mu s_h = 0$ implies that $s_h = 1$ and $\frac{ds_m}{dt} = \eta - \eta s_m = 0$ implies that $s_m = 1$. Thus, the disease-free equilibrium point of the model is given by $E_0 = (1, 0, 0, 0, 1, 0)$.

1.2. Basic Reproduction number R_0

The reproduction number is defined as the average number of secondary cases produced by a typical infected individual during his or her entire life as infectious or infectious period when introduced or allowed to live in a population of susceptible [13].Now we compute the basic reproduction number $R_0$of the present model using the next generation matrix method described by Diekmann, Heesterbeek, and Metz in [4].In the dynamical system (12)−(17) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals $\mathcal{V}$ at the disease-free steady state $E_0 = (1,0,0,0,1,0)$gives the Jacobian matrices $\begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix}$and $\begin{bmatrix} V & 0 \\ J_3 & J_4 \end{bmatrix}$ where

$$F = \begin{bmatrix} 0 & 0 & 0 & q\beta \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ \alpha_1 & \alpha_2 & 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \delta+\tau+\mu & -r_1 & -r_2 & 0 \\ -\delta & r_1+\gamma+\mu & 0 & 0 \\ -\tau & -\gamma & r_2+\rho+\mu & 0 \\ 0 & 0 & 0 & \eta \end{bmatrix} \text{ with}$$

$$= \frac{1}{\eta[B_1B_2B_3 - r_1\delta B_2 - r_2[\delta\gamma + \tau B_1]]} \begin{pmatrix} \eta B_1 B_2 & \eta[r_1B_2 + r_2\gamma] & \eta r_2 B_1 & 0 \\ \delta\eta B_2 & \eta[B_2B_3 + r_2\tau] & \eta r_2\delta & 0 \\ \eta[\delta\gamma + \tau B_1] & \eta[\gamma B_3 + r_1\tau] & \eta[B_3B_1 - r_1\delta] & 0 \\ 0 & 0 & 0 & B_1B_2B_3 - r_1\delta B_2 - r_2[\delta\gamma + \tau B_1] \end{pmatrix}$$

Thus the spectral radius or Eigenvalue of $FV^{-1}$is the required basic reproduction number obtained by $R_0 = \sqrt{\frac{q\beta(r_2+\rho+\mu)[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}{\eta(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-\eta r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}}$.

Local Stability of the disease-free equilibrium point E_0

Theorem

For the system of differential equations (12) *to* (17), the disease-free equilibrium point $E_0 = (1, 0, 0, 0, 1, 0)$is locally asymptotically stable if $R_0 < 1$.

Proof

The Jacobian matrix of the dynamical system(12) −(17) at the disease-free equilibrium point $E_0 = (1, 0, 0, 0, 1, 0)$is

$$J(1,0,0,0,1,0) = \begin{pmatrix} -\mu & 0 & 0 & \rho & 0 & -q\beta \\ 0 & -(\delta+\tau+\mu) & r_1 & r_2 & 0 & q\beta \\ 0 & \delta & -(r_1+\gamma+\mu) & 0 & 0 & 0 \\ 0 & \tau & \gamma & -(r_2+\rho+\mu) & 0 & 0 \\ 0 & -\alpha_1 & -\alpha_2 & 0 & -\eta & 0 \\ 0 & \alpha_1 & \alpha_2 & 0 & 0 & -\eta \end{pmatrix}$$

Whose characteristic equation with eigenvalue λ is

$$\begin{vmatrix} -\mu-\lambda & 0 & 0 & \rho & 0 & -q\beta \\ 0 & -(\delta+\tau+\mu)-\lambda & r_1 & r_2 & 0 & q\beta \\ 0 & \delta & -(r_1+\gamma+\mu)-\lambda & 0 & 0 & 0 \\ 0 & \tau & \gamma & -(r_2+\rho+\mu)-\lambda & 0 & 0 \\ 0 & -\alpha_1 & -\alpha_2 & 0 & -\eta-\lambda & 0 \\ 0 & \alpha_1 & \alpha_2 & 0 & 0 & -\eta-\lambda \end{vmatrix} = 0$$

Whose eigenvalues are $\lambda_1 = -\mu \quad or \quad \lambda_2 = -\eta$ or the other four eigenvalues are the roots of the characteristic equation

$$\begin{vmatrix} -(\delta+\tau+\mu)-\lambda & r_1 & r_2 & q\beta \\ \delta & -(r_1+\gamma+\mu)-\lambda & 0 & 0 \\ \tau & \gamma & -(r_2+\rho+\mu)-\lambda & 0 \\ \alpha_1 & \alpha_2 & 0 & -\eta-\lambda \end{vmatrix} = 0 \text{ or we do have}$$

$$\lambda^4 + [(r_1+\gamma+\mu)+(r_2+\rho+\mu)+(\delta+\tau+\mu)+\eta]\lambda^3 + [(r_1+\gamma+\mu)(r_2+\rho+\mu)+(r_1+\gamma+\mu)(\delta+\tau+\mu)+(r_2+\rho+\mu)(\delta+\tau+\mu) + (r_1+\gamma+\mu)\eta+(r_2+\rho+\mu)\eta+(\delta+\tau+\mu)\eta-\delta r_1-\tau r_2-q\beta\alpha_1]\lambda^2 + [-\tau r_2\eta + (r_2+\rho+\mu)(\delta+\tau+\mu)\eta-q\beta\alpha_1(r_2+\rho+\mu)-(r_1+\gamma+\mu)\tau r_2 + (r_1+\gamma+\mu)(r_2+\rho+\mu)(\delta+\tau+\mu)+(r_1+\gamma+\mu)(r_2+\rho+\mu)\eta + (r_1+\gamma+\mu)(\delta+\tau+\mu)\eta-q\beta\alpha_1(r_1+\gamma+\mu)-\delta\gamma r_2-\delta(r_2+\rho+\mu)r_1-\delta r_1\eta - \delta q\beta\alpha_2]\lambda-\delta\gamma r_2\eta-\delta(r_2+\rho+\mu)r_1\eta-\delta q\beta\alpha_2(r_2+\rho+\mu)-(r_1+\gamma+\mu)\tau r_2\eta + (r_1+\gamma+\mu)(r_2+\rho+\mu)(\delta+\tau+\mu)\eta-(r_1+\gamma+\mu)(r_2+\rho+\mu)q\beta\alpha_1 = 0$$

To evaluate the signs of the roots of this fourth-degree polynomial equation we used the Routh Hurwitz criterion. Using the Routh-Hurwitz stability criterion we prove that when $R_0 < 1$ all roots of the fourth-degree polynomial equation have negative real parts. Thus the disease-free equilibrium point $E_0$is locally asymptotically stable if $R_0 < 1$.

Global stability of disease-free equilibrium

Theorem

For the dynamical system (12) to (17) the disease-free equilibrium $E_0 = (1,0,0,0,1,0)$is globally asymptotically stable if $R_0 < 1$.

Proof

To prove the global asymptotic stability of the disease free equilibrium E_0 we use the method of Lyapunov functions and we defined a Lyapunov function by $V = a_1 i_h + a_2 t_h + a_3 r_h + a_4 i_m where\ a_i\ ;\ i = 1,2,3,4$ are positive constants to be determined and we have observe that the determined Lyapunov function is continuous. Then the time derivative of $V$is given by$\frac{dV}{dt} = a_1\frac{di_h}{dt} + a_2\frac{dt_h}{dt} + a_3\frac{dr_h}{dt} + a_4\frac{di_m}{dt}$. By substituting expressions for $\frac{di_h}{dt}, \frac{dt_h}{dt}, \frac{dr_h}{dt}, and\ \frac{di_m}{dt}$ from the system (12)−(17) and after some simplification we get

$$\frac{dV}{dt} = \begin{Bmatrix} a_1[q\beta(1-i_h-t_h-r_h)i_m + r_1 t_h + r_2 r_h - (\delta+\tau+\mu)i_h] + a_2[\delta i_h - (r_1+\gamma+\mu)t_h] + \\ a_3[\gamma t_h + \tau i_h - (r_2+\rho+\mu)r_h] + a_4[\alpha_1(1-i_m)i_h + \alpha_2(1-i_m)t_h - \eta i_m] \end{Bmatrix}$$

And after some simplification we do have when $R_0 < 1$ we get $\frac{dV}{dt} \le 0$ and furthermore $\frac{dV}{dt} = 0$ only if $i_m = 0$ which leads to $i_h = 0,\ t_h = 0,\ r_h = 0$ and also leads to $s_h = 1\ and\ s_m = 1$. Hence the disease free equilibrium point E_0 is globally asymptotically stable.

1.3. Endemic equilibrium point

An endemic equilibrium point is steady state solution where the disease persists in the population.For thedynamical system(12)−(17) we find an explicit representation of the endemic equilibrium point $E^* = (s_h^*, i_h^*, t_h^*, r_h^*,\ s_m^*, i_m^*)$ where

$$s_h^* = 1 - \left(i_h^* + \frac{\delta}{r_1+\gamma+\mu}i_h^* + \frac{\gamma\delta+\tau(r_1+\gamma+\mu)}{(r_1+\gamma+\mu)(r_2+\rho+\mu)}i_h^*\right)$$

$$i_h^* = \frac{\eta B_1[B_1B_2B_3 - r_1\delta B_2 - r_2(\gamma\delta+\tau B_1)]\times(R_0^2-1)}{q\beta\,(B_1B_2+\delta B_2+\gamma\delta-\tau B_1)(\alpha_1B_1+\alpha_2\delta)+[B_1B_2B_3-r_1\delta B_2-r_2(\gamma\delta+\tau B_1)](\alpha_1B_1+\alpha_2\delta)}$$

$$t_h^* = \frac{\delta}{r_1+\gamma+\mu}i_h^*$$

$$r_h^* = \frac{\gamma\delta+\tau(r_1+\gamma+\mu)}{(r_1+\gamma+\mu)(r_2+\rho+\mu)}i_h^*$$

$$s_m^* = 1 - \left(\frac{[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]i_h^*}{[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]i_h^*+\eta(r_1+\gamma+\mu)}\right)$$

$$i_m^* = \frac{[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]i_h^*}{[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]i_h^*+\eta(r_1+\gamma+\mu)} \text{with} B_1 = r_1+\gamma+\mu\ ,\ B_2 = r_2+\rho+\mu, \text{ and } B_3 = \delta+\tau+\mu$$

Local stability of the endemic equilibrium point

Theorem

For system (12) to (17)the endemic equilibrium $E^* = (s_h^*, i_h^*, t_h^*, r_h^*,\ s_m^*, i_m^*)$is locally asymptotically stable if $R_0 > 1$.

Proof

The Jacobian matrix of the dynamical system (12) *to* (17) at the endemic equilibrium point $(s_h^*, i_h^*, t_h^*, r_h^*, s_m^*, i_m^*)$ is

$$\begin{pmatrix} -q\beta i_m^* - \mu & 0 & 0 & \rho & 0 & -q\beta s_h^* \\ q\beta i_m^* & -(\delta+\tau+\mu) & r_1 & r_2 & 0 & q\beta s_h^* \\ 0 & \delta & -(r_1+\gamma+\mu) & 0 & 0 & 0 \\ 0 & \tau & \gamma & -(r_2+\rho+\mu) & 0 & 0 \\ 0 & -\alpha_1 s_m^* & -\alpha_2 s_m^* & 0 & -\alpha_1 i_h^* - \alpha_2 t_h^* - \eta & 0 \\ 0 & \alpha_1 s_m^* & \alpha_2 s_m^* & 0 & \alpha_1 i_h^* + \alpha_2 t_h^* & -\eta \end{pmatrix}$$

The corresponding characteristic polynomial with eigenvalue $\lambda$is

$$\begin{vmatrix} -q\beta i_m^* - \mu - \lambda & 0 & 0 & \rho & 0 & -q\beta s_h^* \\ q\beta i_m^* & -(\delta+\tau+\mu) - \lambda & r_1 & r_2 & 0 & q\beta s_h^* \\ 0 & \delta & -(r_1+\gamma+\mu) - \lambda & 0 & 0 & 0 \\ 0 & \tau & \gamma & -(r_2+\rho+\mu) - \lambda & 0 & 0 \\ 0 & -\alpha_1 s_m^* & -\alpha_2 s_m^* & 0 & -\alpha_1 i_h^* - \alpha_2 t_h^* - \eta - \lambda & 0 \\ 0 & \alpha_1 s_m^* & \alpha_2 s_m^* & 0 & \alpha_1 i_h^* + \alpha_2 t_h^* & -\eta - \lambda \end{vmatrix} = 0$$

Or we can rewrite this equation

$$\begin{vmatrix} -a_1 - \lambda & 0 & 0 & a_4 & 0 & -a_6 \\ b_1 & -b_2 - \lambda & b_3 & b_4 & 0 & b_6 \\ 0 & c_2 & -c_3 - \lambda & 0 & 0 & 0 \\ 0 & d_2 & d_3 & -d_4 - \lambda & 0 & 0 \\ 0 & -e_2 & -e_3 & 0 & -e_5 - \lambda & 0 \\ 0 & f_2 & f_3 & 0 & f_5 & -f_6 - \lambda \end{vmatrix} = 0$$

Where

$a_1 = q\beta i_m^* + \mu, \quad a_2 = a_3 = a_5 = 0, \quad a_4 = \rho, a_6 = q\beta s_h^*, \quad b_1 = q\beta i_m^*, b_2 = \delta + \tau + \mu, \quad b_3 = r_1, \quad b_4 = r_2, b_5 = 0, b_6 = q\beta s_h^*, c_1 = c_4 = c_5 = c_6 = 0, \; c_2 = \delta, \; c_3 = r_1 + \gamma + \mu, \; d_1 = d_5 = d_6 = 0, \quad d_2 = \tau, \; d_3 = \gamma, d_4 = r_2 + \rho + \mu, e_1 = e_4 = e_6 = 0, \quad e_2 = \alpha_1 s_m^*, e_3 = \alpha_2 s_m^*, e_5 = \alpha_1 i_h^* + \alpha_2 t_h^* + \eta, \; f_1 = f_4 = 0, f_2 = \alpha_1 s_m^*, f_3 = \alpha_2 s_m^*, f_5 = \alpha_1 i_h^* + \alpha_2 t_h^* f_6 = \eta.$

This characteristic equation can be written in the form of

$A_6\lambda^6 + A_5\lambda^5 + A_4\lambda^4 + A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0$

Where $A_6 = 1$

$A_5 = a_1 + b_2 + c_3 + d_4$

$A_4 = e_5f_6 + (e_5 + f_6) - c_2b_3 - b_4d_2 + d_4b_2 + a_1b_2 + c_3b_2 + a_1d_4 + c_3d_4 + a_1c_3 - b_6f_2$

$A_3 = b_2e_5f_6 + d_4e_5f_6 + a_1e_5f_6 + c_3e_5f_6 + (e_5 + f_6)b_2 + (e_5 + f_6)d_4 + (e_5 + f_6)a_1 + (e_5 + f_6)c_3 - c_2b_4d_3 - c_2b_3a_1 - c_2b_3d_4 - b_4d_2a_1 - b_4d_2c_3 + d_4b_2a_1 + d_4b_2c_3 + a_1c_3b_2 + a_1c_3d_4 - b_1a_4d_2 - c_2b_6f_3 - b_6e_2f_6 - b_6d_4f_2 - b_6a_1f_2 - b_6c_3f_2 + b_1a_6f_2$

$A_2 = -c_2b_3e_5f_6 - b_4d_2e_5f_6 + d_4b_2e_5f_6 + a_1b_2e_5f_6 + c_3b_2e_5f_6 + a_1d_4e_5f_6 + c_3d_4e_5f_6 + a_1c_3e_5f_6 - (e_5 + f_6)c_2b_3 - (e_5 + f_6)b_4d_2 + (e_5 + f_6)d_4b_2 + (e_5 + f_6)a_1b_2 + (e_5 + f_6)c_3b_2 + (e_5 + f_6)a_1d_4 + (e_5 + f_6)c_3d_4 + (e_5 + f_6)a_1c_3 - a_1c_2b_4d_3 - c_2b_3a_1d_4 - b_4d_2a_1c_3 + a_1c_3d_4b_2 - b_1a_4c_2d_3 - b_1c_3a_4d_2 - c_2b_6e_3f_6 - c_2b_6a_1f_3 - c_2b_6d_4f_3 + b_1a_6c_2f_3 - b_6d_4e_2f_6 - b_6a_1e_2f_6 - b_6c_3e_2f_6 + b_1a_6e_2f_6 - b_6a_1d_4f_2 - b_6c_3d_4f_2 - b_6a_1c_3f_2 + b_1a_6c_3f_2 + b_1a_6d_4f_2$

$A_1 = -c_2b_4d_3e_5f_6 - c_2b_3a_1e_5f_6 - c_2b_3d_4e_5f_6 - b_4d_2a_1e_5f_6 - b_4d_2c_3e_5f_6 + d_4b_2a_1e_5f_6 + d_4b_2c_3e_5f_6 + a_1c_3b_2e_5f_6 + a_1c_3d_4e_5f_6 - b_1a_4d_2e_5f_6 - (e_5 + f_6)c_2b_4d_3 - (e_5 + f_6)c_2b_3a_1 - (e_5 + f_6)c_2b_3d_4 - (e_5 + f_6)b_4d_2a_1 - (e_5 + f_6)b_4d_2c_3 + (e_5 + f_6)d_4b_2a_1 + (e_5 + f_6)d_4b_2c_3 + (e_5 + f_6)a_1c_3b_2 + (e_5 + f_6)a_1c_3d_4 - (e_5 + f_6)b_1a_4d_2 - c_2b_6a_1e_3f_6 - c_2b_6d_4e_3f_6 + b_1a_6c_2e_3f_6 - c_2b_6a_1d_4f_3 + b_1a_6c_2d_4f_3 - b_6a_1d_4e_2f_6 - b_6c_3d_4e_2f_6 - b_6a_1c_3e_2f_6 + b_1a_6c_3e_2f_6 + b_1a_6d_4e_2f_6 - b_6a_1c_3d_4f_2 + b_1a_6c_3d_4f_2$

$A_0 = -a_1c_2b_4d_3e_5f_6 - c_2b_3a_1d_4e_5f_6 - b_4d_2a_1c_3e_5f_6 + a_1b_2c_3d_4e_5f_6 - b_1a_4c_2d_3e_5f_6 - b_1c_3a_4d_2e_5f_6 - (e_5 + f_6)a_1c_2b_4d_3 - (e_5 + f_6)c_2b_3a_1d_4 - (e_5 + f_6)b_4d_2a_1c_3 + (e_5 + f_6)a_1c_3d_4b_2 - (e_5 + f_6)b_1a_4c_2d_3 - (e_5 + f_6)b_1c_3a_4d_2 - c_2b_6a_1d_4e_3f_6 + b_1a_6c_2d_4e_3f_6 - b_6a_1c_3d_4e_2f_6 + b_1a_6c_3d_4e_2f_6$

Using Routh-Hurwitz stability criterionwe find that when $R_0 > 1$all the eigenvalues of this characteristic equation are negative. Thus, the endemic equilibrium point is locally asymptotically stable for$R_0 > 1$.

Global stability of the endemic equilibrium point

Theorem

If $R_0 > 1$ the endemic equilibrium point$E^* = (s_h^*,\ i_h^*,\ t_h^*,\ r_h^*,\ s_m^*,\ i_m^*)$ of the dynamical system (12) − (17) is globally asymptotically stable.

Proof

We define an appropriate Lyapunov function by

$$V(X) = \begin{Bmatrix} \left(i_h - i_h^* - i_h^* \, ln\left(\frac{i_h}{i_h^*}\right)\right) + \left(t_h - t_h^* - t_h^* \, ln\left(\frac{t_h}{t_h^*}\right)\right) + \\ \left(r_h - r_h^* - r_h^* \, ln\left(\frac{r_h}{r_h^*}\right)\right) + \left(i_m - i_m^* - i_m^* \, ln\left(\frac{i_m}{i_m^*}\right)\right) \end{Bmatrix}$$

And we have observed that the determined Lyapunov function is continuous. Then differentiating with respect to time $t$gives

$$\frac{dV}{dt} = \left(1 - \frac{i_h^*}{i_h}\right)\frac{di_h}{dt} + \left(1 - \frac{t_h^*}{t_h}\right)\frac{dt_h}{dt} + \left(1 - \frac{r_h^*}{r_h}\right)\frac{dr_h}{dt} + \left(1 - \frac{i_m^*}{i_m}\right)\frac{di_m}{dt}$$

By replacing$\frac{di_h}{dt}$, $\frac{dt_h}{dt}$, $\frac{dr_h}{dt}, and\ \frac{di_m}{dt}$in this equation from their respective expressions fromthe dynamical system (12)− (17) we get

$$\frac{dV}{dt} = \left(1 - \frac{i_h^*}{i_h}\right)[q\beta(1 - i_h - t_h - r_h)i_m + r_1 t_h + r_2 r_h - (\delta + \tau + \mu)i_h] + \left(1 - \frac{t_h^*}{t_h}\right)[\delta i_h - (r_1 + \gamma + \mu)t_h] +$$

$$\left(1 - \frac{r_h^*}{r_h}\right)[\gamma t_h + \tau i_h - (r_2 + \rho + \mu)r_h] + \left(1 - \frac{i_m^*}{i_m}\right)[\alpha_1(1 - i_m)i_h + \alpha_2(1 - i_m)t_h - \eta i_m]$$

Then $\frac{dV}{dt} \leq 0, and\ \frac{dV}{dt} = 0$ if and only if $i_h = i_h^*,\ t_h = t_h^*, r_h = r_h^*, i_m = i_m^*,\ s_h = s_h^*\ and$ $s_m = s_m^*$. therefore the endemic equilibrium point E^* is globally asymptotically stable.

III. Parameter Estimation for Numerical Simulation and Sensitivity Analysis

To perform numerical simulation and sensitivity analysis we collect the following parameter values obtained from different sources.

Parameter	Meaning	Value	Unit	Source
α_1	From an infectious human to a susceptible mosquito, transmission rate in mosquitoes	0.8333	day^{-1}	[7]
α_2	From a treated human to a susceptible mosquito, transmission rate in mosquitoes	0.0833	day^{-1}	[7]
β	From an infectious mosquito to a susceptible human, transmission rate in humans	$2*10^{-2}$	day^{-1}	[7]
N	The total size of human population	Estimated		Estimated
M	The total size of mosquito population	qN		Calculated
μ	Natural birth and death rate of humans	1/70	$year^{-1}$	[7]
δ	Treatment rate	0.01	day^{-1}	[8]
r_1	From a treated human to an infectious human, relapse rate	0.01	day^{-1}	Estimated
r_2	From a recovered human to an infectious human, relapse rate	0.004	day^{-1}	[7]
γ	From a treated human to a recovered human, recovery rate	0.00722	day^{-1}	[8]
ρ	From a recovered human to a susceptible human, rate of loss of immunity	0.0146	day^{-1}	[7]
τ	From an infectious human to a recovered human, recovery rate	0.142	day^{-1}	[8]
η	Natural birth and death rate of mosquitoes	0.1429	day^{-1}	[7]
q	The number of mosquitoes per individual	1-2		[7]

Table 2. Description of parameters and parameter values

Estimation of basic reproduction number R_0

The basic reproduction numberR_0 of the dynamical system is obtained as

$R_0 = \sqrt{\frac{q\beta(r_2+\rho+\mu)[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}{\eta(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-\eta r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}}$. Thus, using the standard data given in Table 2the numerical value of basic reproduction number$R_0 = 1.2736$.

Numerical simulation

The numerical analysis is obtained from the graphs of basic reproduction number with respect to the parameters obtained and given in Table 2.

Rate of transmission of the disease from an infectious mosquito to a susceptible human β

Graphical representation of the basic reproduction number R_0 versus rate of transmission of the disease from an infectious mosquito to a susceptible human β and keeping other parameters constant

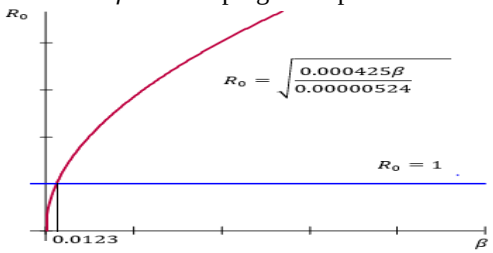

Figure 2: From this graphwe can observe that an increase in the rate of transmission of the disease from an infectious mosquito to a susceptible humanβ, between 0 and 0.0123, makes an increase in the reproduction number with, $R_0 < 1$ and tell us the disease not persists. Whereas, the rate of transmission greater than 0.0123, makes an increase in the reproduction number with $R_0 > 1$ and tell us the disease persists.

Recovery rate from an infectious human to a recovered human τ

Graphical representation of the basic reproduction number R_0 versus recovery rate from an infectious human to a recovered human τ and keeping other parameters constant

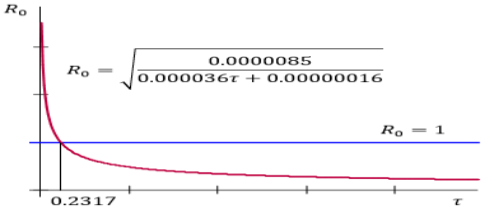

Figure 3: From this figure we can observe that an increase in the rate of recovery τ, from an infectious human to a recovered human, between 0 and 0.2317, makes a decrease in the reproduction number with $R_0 > 1$ and tell us the disease persists. If the rate of recovery τ, from an infectious human to a recovered human greater than 0.2317 makes a decrease in the reproduction number with, $R_0 < 1$ and tell us the disease dies out.

Transmission ratefrom an infectious human to a susceptible mosquito α_1

Graphical representation of the basic reproduction number R_0 versus transmission rate in mosquitoes from an infectious human to a susceptible mosquito $\alpha_1$and keeping other parameters constant

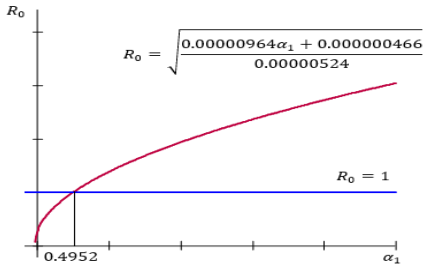

Figure 4: From this figure we can observe that an increase in the rate of transmission of the disease from an infectious human to a susceptible mosquitoα_1, between 0 and 0.4952, makes an increase in the reproduction number with, $R_0 < 1$ and tell us the disease not persists. Whereas, the rate of transmission greater than 0.4952, makes an increase in the reproduction number, $R_0 > 1$ and tell us the disease persists.

Transmission rate from a treated human to a susceptible mosquito α_2

Graphical representation of the basic reproduction number R_0 versus transmission rate in mosquitoes from a treated human to a susceptible mosquito $\alpha_2$and keeping other parameters constant.

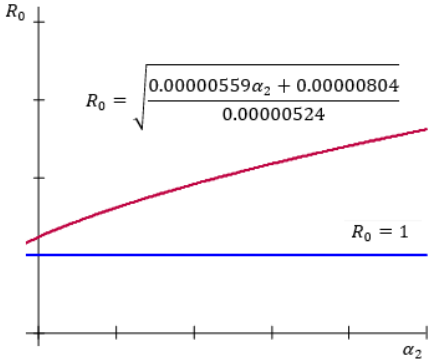

Figure 5: From this figure we can observe that an increase in the rate of transmission of the disease from a treated human to a susceptible mosquito, α_2, makes an increase in the reproduction number, $R_0 > 1$ and tell us the disease persists. That is the disease always persists for any value of parameter α_2.

Treatment rate δ

Graphical representation of the basic reproduction number R_0 versus treatment rate δ and keeping other parameters constant

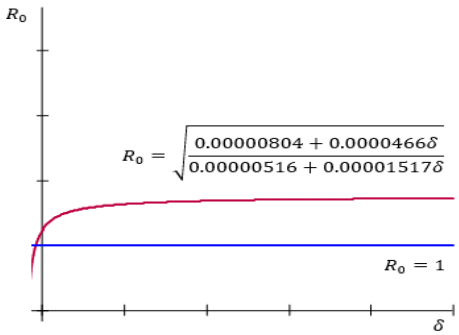

Figure 6: From this figure we can observe that an increase in the treatment rate δ,then the reproduction number almost constant with $R_0 > 1$ and tell us the disease still persists.

Relapse rate from the treated human to an infectious humanr_1

Graphical representation of the basic reproduction number R_0 versus relapse rate from the treated human to an infectious human$r_1$and keeping other parameters constant

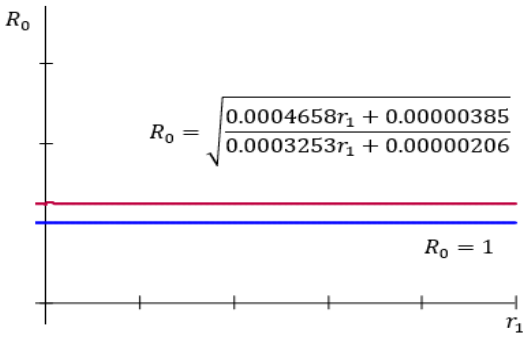

Figure 7: From this figure we can observe that an increase in the relapse rate,r_1, from the treated human to an infectious human, then the reproduction number almost constant, with $R_0 > 1$ and tell us the disease still persists with constant reproduction number (i.e. approximately 1.8689).

Relapse rate from the recovered human to an infectious human r_2

Graphical representation of the basic reproduction number R_0 versus Relapse rate from the recovered human to an infectious human r_2 and keeping other parameters constant

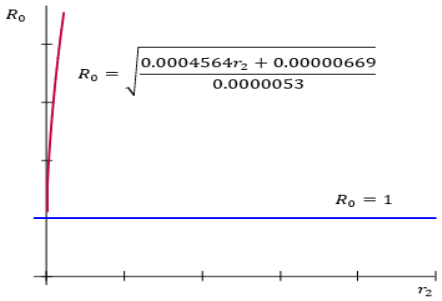

Figure 8: From this figure we can observe that an increase in the rate of relapse,r_2, from the recovered human to an infectious human, makes an increase in the reproduction number, $R_0 > 1$ and tell us the disease persists.

Rate of loss of immunity from a recovered human to a susceptible human ρ

Graphical representation of the basic reproduction number R_0 versus rate of loss of immunity from a recovered human to a susceptible human ρ and keeping other parameters constant

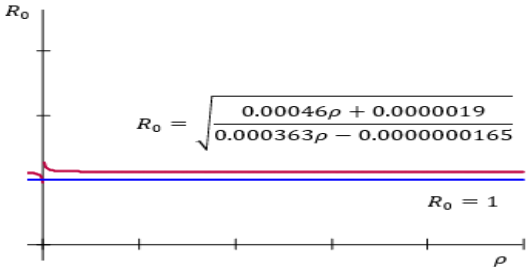

Figure 9: From this figure we can observe that an increase in the rate of loss of immunity, ρ, from a recovered human to a susceptible human, then the reproduction number almost constant, with $R_0 > 1$ and tell us the disease still persists with constant reproduction number.

Recovery rate from a treated human to a recovered human γ

Graphical representation of the basic reproduction number R_0 versus recovery rate from a treated human to a recovered human $\gamma$and keeping other parameters constant

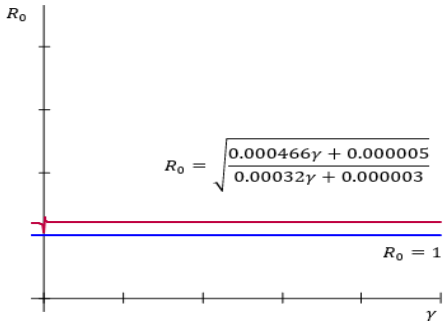

Figure 10: From this figure we can observe that an increase in the recovery rate, γ, from a treated human to a recovered human, then the reproduction number almost constant with $R_0 > 1$ and tell us the disease still persists with constant reproduction number.

IV. Sensitivity Analysis

Sensitivity analysis is helpful for experimental design, data assimilation and reduction of complex non-linear models. Values for sensitivity indices indicate which parameters should be targeted most for interventions purposes. A very high sensitivity index indicates that more care should be taken in the estimation of the associated parameter. The normalized forward sensitivity index is often used to determine the parameters that have higher influence on the basic reproduction numberR_0.The normalized forward sensitivity index of a variable, u, that depends differentiallyon a parameter, p, is defined as$SI_p^u = \frac{\partial u}{\partial p}\frac{p}{u}$. If the magnitude of sensitivityindex is high for the parameter p out of other parameters then we say that p is more sensitive parameter. In this work we consider parameters $\alpha_1, \alpha_2, \beta, r_1, r_2, \delta, \rho, \tau, \mu, \gamma, and\ \eta$ to see the sensitivity parameter with regard to basic reproduction number R_0 as follows. To minimize the complexity of the calculation let ${R_0}^2 = \frac{Y}{X}$, where $Y = q\beta(r_2 + \rho + \mu)[\alpha_1(r_1 + \gamma + \mu) + \alpha_2\delta], and$

$$X = \eta(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu) - r_1\delta] - \eta r_2[\gamma\delta + \tau(r_1+\gamma+\mu)]$$

$$SI_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \beta}\right) \times \frac{\beta}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{{R_0}^2}{\beta}\right) \times \frac{\beta}{R_0} = \frac{1}{2}$$

$$SI_{\eta}^{R_0} = \frac{\partial R_0}{\partial \eta} \times \frac{\eta}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \eta}\right) \times \frac{\eta}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{{R_0}^2}{\eta}\right) \times \frac{\eta}{R_0} = \frac{1}{2}$$

$$SI_{\alpha_1}^{R_0} = \frac{\partial R_0}{\partial \alpha_1} \times \frac{\alpha_1}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \alpha_1}\right) \times \frac{\alpha_1}{R_0} = \frac{\alpha_1(r_1+\gamma+\mu)}{2[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}$$

$$SI_{\alpha_2}^{R_0} = \frac{\partial R_0}{\partial \alpha_2} \times \frac{\alpha_2}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \alpha_2}\right) \times \frac{\alpha_2}{R_0} = \frac{\alpha_2\delta}{2[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}$$

$$SI_{r_1}^{R_0} = \frac{\partial R_0}{\partial r_1} \times \frac{r_1}{R_0} = \frac{r_1\alpha_1}{2[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]} - \frac{r_1[\eta(r_2+\rho+\mu)(\delta+\tau+\mu)-\eta(r_2+\rho+\mu)\delta-\eta r_2\tau]}{2[\eta(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-\eta r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]]}$$

$$SI_{r_2}^{R_0} = \frac{\partial R_0}{\partial r_2} \times \frac{r_2}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial r_2}\right) \times \frac{r_2}{R_0} = \frac{r_2}{2(r_2+\rho+\mu)} - \frac{r_2\eta[(r_1+\gamma+\mu)(\delta+\tau+\mu)-(r_1+\gamma+\mu)\delta-\gamma\delta-\tau(r_1+\gamma+\mu)]}{2X}$$

$$SI_{\delta}^{R_0} = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \delta}\right) \times \frac{\delta}{R_0} = \frac{q\beta\delta\,\alpha_2(r_2+\rho+\mu)}{2Y} - \frac{\eta\delta\,[(r_1+\gamma+\mu)(r_2+\rho+\mu)-r_1(r_2+\rho+\mu)-r_2\gamma]}{2X}$$

$$SI_{\gamma}^{R_0} = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \gamma}\right) \times \frac{\gamma}{R_0} = \frac{q\beta\gamma\,\alpha_1(r_2+\rho+\mu)}{2Y} - \frac{\eta\gamma\,[(r_2+\rho+\mu)(\delta+\tau+\mu)-r_2\delta-r_2\tau]}{2X}$$

$$SI_{\tau}^{R_0} = \frac{\partial R_0}{\partial \tau} \times \frac{\tau}{R_0} = \left(\frac{1}{2R_0}\right)\left(\frac{\partial {R_0}^2}{\partial \tau}\right) \times \frac{\tau}{R_0} = \frac{\tau(r_1+\gamma+\mu)[r_2-(r_2+\rho+\mu)]}{2(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-2r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}$$

$$SI_{\rho}^{R_0} = \frac{\partial R_0}{\partial \rho} \times \frac{\rho}{R_0} = \frac{\rho}{2(r_2+\rho+\mu)} - \frac{\rho[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]}{2(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}$$

$$SI_{\mu}^{R_0} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = \frac{\mu[\alpha_1(r_2+\rho+\mu)+\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]}{2(r_2+\rho+\mu)[\alpha_1(r_1+\gamma+\mu)+\alpha_2\delta]} - \frac{\mu[(r_2+\rho+\mu)[(r_1+\gamma+\mu)+(\delta+\tau+\mu)]+(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_2\tau]}{2(r_2+\rho+\mu)[(r_1+\gamma+\mu)(\delta+\tau+\mu)-r_1\delta]-r_2[\gamma\delta+\tau(r_1+\gamma+\mu)]}$$

Using the data in table 2 the resulting sensitivity indices of R_0 to the eleven different parameters in the model are shown in the following table

Parameter	Sensitivity Index
τ	-0.517
β	0.5
η	0.5
α_1	0.47256
ρ	-0.1383
r_2	0.1114
γ	-0.03
α_2	0.02737
δ	0.012412
r_1	-0.01092
μ	-0.000814

Table 3: This table contains positive and negative sensitivity indices. The parameters are ordered from most sensitive to least.

V. Results and Discussion

Results from Numerical simulation show that an increase in the rate of transmission of the disease from an infectious mosquito to a susceptible humanβ, between 0 and 0.0123, makes an increase in the reproduction number with, $R_0 < 1$ and tell us the disease not persists. Whereas, the rate of transmission greater than 0.0123, makes an increase in the reproduction number, $R_0 > 1$ and tell us the malaria disease persists. We can observe that an increase in the human recovery rate, τ, from an infectious human to a recovered human, between 0 and 0.2317, makes a decrease in the reproduction number, with $R_0 > 1$ and tell us the disease persists. If the rate of recovery, τ, from an infectious human to a recovered human greater than 0.2317 makes a decrease in the reproduction number with, $R_0 < 1$ and tell us the disease dies out.Whereas either the treatment rate δ, or the recovery rate γ, from a treated human to a recovered human does not reduce the reproduction number.

An increase in the rate of transmission of the disease from an infectious human to a susceptible mosquitoα_1, between 0 and 0.4952, makes an increase in the reproduction number with, $R_0 < 1$ and tell us the disease not persists. Whereas, the rate of transmission greater than 0.4952, makes an increase in the reproduction number with $R_0 > 1$ and tell us the disease persists. We can observe that an increase in the rate of transmission of the disease from a treated human to a susceptible mosquito α_2, and the rate of relapsefrom the recovered human to an infectious human r_2, makes an increase in the reproduction number, with the reproduction number greater than one, and tell us the disease persists. Also, an increase in the rate of loss of immunity ρ, and the relapse rate, from the treated human to an infectious humanr_1, then the reproduction

number almost constant, but the reproduction number is greater than one and tell us the disease still persists with constant reproduction number.

From sensitive analysis we observed that the most sensitive parameter is the human recovery rateτ, from an infectious human to a recovered human. Other important parameters include the transmission rate in humansfrom an infectious mosquito to a susceptible human, β the transmission rate in mosquitoes from an infectious human to a susceptible mosquitoα_1, and the mosquitoes' natural birth and death rate η. The least sensitive parameter is the natural birth and death rate of humans μ. The indices having positive signs increase the value of R_0as one increase them and those having negative signs decrease the value ofR_0, when they are increased.

VI. Conclusion

In this paper, we analyzed an ordinary differential equation model for the transmission of malaria, with four variables for humans and two variables for mosquitoes. We showed that there exists a domain where the model is epidemiologically and mathematically well-posed. We obtained the disease-free equilibrium point E_0 and a unique endemic equilibrium pointE^*. We defined a reproduction number R_0, for our model that it provides the expected number of new infections from one infectious individual over the duration of the infectious period, given that all other members of the population are susceptible.

The stability analysis on the model shows that the disease-free equilibrium point E_0 is shown to be locally asymptotically stable and globally asymptotically stable when $R_0 < 1$ and the positive endemic equilibrium point E^* is shown to be locally asymptotically stable and globally asymptotically stable when $R_0 > 1$. A sensitivity analysis of the basic reproduction number, which allows us to determine the relative importance of the parameters to the disease transmission and prevalence, indicates that the most sensitive parameter is the human recovery rate from an infectious human to a recovered human τ . Other important parameters include the transmission rate in humansfrom an infectious mosquito to a susceptible human β , the transmission rate in mosquitoes from an infectious human to a susceptible mosquitoα_1, and the of mosquitoes natural birth and death rate η.

Results from numerical simulation show that as the rate of transmission in human and in mosquito increases, the basic reproduction number also increases. This will result in increasing on the transmission of malaria. The human recovery rate and the mosquito natural birth and death rate increases, the basic reproduction number also increases. This will result in decreasing on the transmission and prevalence of malaria.

Recommendation

From the above results and discussion, we would like to recommend the following to control the spread of malaria: The most sensitive parameters like human recovery rate, human and mosquito transmission rates, and the mosquito birth and death rate, should be targeted by policy makers in developing the natural recovery of the person and reducing the number of contacts between humans and mosquitoes, keep the human recovery rate τ, greater than 0.2317, where the reproduction number is less than one, keep the rate of transmission in human β, less than 0.0123, keepthe rate of transmission in mosquito less than 0.4952 and keepthe natural mosquito death rate greater than 0.2291.

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