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LOCAL STABILITY ANALYSIS OF A SUSCEPTIBLE PROTECTED INFECTED TREATED RECOVERED (SPITR) MATHEMATICAL MODEL FOR MALARIA DISEASE DYNAMICS

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Abstract: Malaria is one of the oldest diseases studied for a long time from all angles. 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 the development of a vaccine is underway, it therefore makes it seemingly possible to reduce the susceptible class through vaccination. In this paper, we have investigated and modify an SPITR mathematical model of Fekadu*et al*. for the transmission and control of malaria disease by incorporating parameters for vaccination and vector reduction and as well, determine the basic reproduction number of the model. We showed that the disease free equilibrium (DFE) state is locally asymptotically stable if $R_o < 1$ and unstable if greater than unity. This shows that if $R_o < 1$, malaria can be controlled in the population.

Keywords: Basic reproduction number,Jacobian matrix, malaria, next generation matrix

Introduction

Malaria, formerly called ague fever, is one of the most common infectious diseases which pose a major health challenge for human beings worldwide (Marsh, 1998). Malaria is the common name and it is caused by single-celled parasites of the genus Plasmodium. Among these parasites, five species have been identified as potential causes of the disease in human. These are: Plasmodium vivax, Plasmodium malariae, Plasmodium falciparum, Plasmodium knowlesi and Plasmodium ovale. Of these, Plasmodium falciparum is of greatest risk to non-immune humans and these accounts for 80% of cases and 90% of deaths (Kakkilaya, 2003). Children under the age of five and pregnant women are the most vulnerable to the severe forms of malaria. Pregnancy lowers the mothers' immunity to malaria making them more susceptible to infection. At present, the disease affects more than 300 million humans and kills 1.5 to 3.0 million people every year (Ngwa and Shu, 2000; Chitnis, 2005; Chitnis, Cushings and Hyman, 2006).

Malaria is transmitted by the bite of an infected female Anopheles mosquito whenever the infected mosquito feeds on blood meal. The symptoms of malaria disease include fever, chills together with headache, vomiting flu-like, anemia (destroying red blood cell), diarrhea, liver and neurological damage. Malaria is endemic in tropical areas where climate and weather conditions allow continuous breeding of the mosquito.

In recent times, various control strategies and intervention programme have been adopted worldwide. Some of which include the introduction of anti-malaria vaccines which is underway, insecticides-treated bed nets (ITNs), internal residual spraying (IRS), control of breeding environment, and biological control among others. These are largely used in malaria endemic countries especially those in Sub-Saharan Africa and have somewhat led to the reduction in the spread of the disease.

Mathematical models play a key role in the control of malaria. Their use in the study of malaria originates from the early work of Ross in 1911 where it was used to prove that bringing the mosquito population below a certain threshold was sufficient to eliminate malaria. This threshold naturally depends on some biological factors such as the biting rate and vectorial capacity. For the purpose of estimating infection and recovery rates, Macdonald (1957) used a model in which he assumed that the amount of infective material upon which a population is exposed remains unaltered. Some epidemiological models as in Aron and May (1982), and Anderson and May (1991) used the assumption that acquired immunity to malaria disease is boosted by additional or continuous exposure to re-infection. In this paper, we modified the SPITR model of Fekadu *et al.* (2015) by including a vaccination and vector reduction parameter in order to determine its impact as a control measure for the spread of malaria.

Definition of terms

Susceptible: The number of individuals who can be infected but have not yet contracted the malaria but may contract it when exposed to its mode of transmission

Protected: The number of individuals from susceptible and recovered compartments who do not and will not contract malaria due to adequate and sufficient preventive measures against possible infection or re-infection. Such preventive measures include vaccination, the use of Indoor Residual Spraying (IRS) and Insecticide Treated Nets (ITNs)

Infected: The number of individuals from susceptible compartment who have been infected of malaria.

Treated: The number of individuals from the infected compartment undergoing clinical treatment after being infected of malaria.

Recovered: The number of individuals from infected and treated compartment who have recovered naturally or clinically and back to normal status of health.

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

WHO: World Health Organization

R_o: The expected number of secondary cases produced by a single (typical) infection in a completely susceptible population

Parameters and variables of the model

Table 1: Parameters and meaning

Parameters	Meaning
ψ	Natural birth rate of humans
ρ	Natural birth rate of mosquito
θ_{mh}	Probability of transmission of malaria from infected mosquito to susceptible human
θ_{hm}	Probability of transmission of malaria from infected human to susceptible mosquito
$\alpha_h = \frac{\theta_{mh}\phi I_m}{N_h}$	Transfer rate of humans from susceptible to infected compartment
$\alpha_m = \frac{\theta_{hm}\phi I_h}{N_h}$	Transfer rate of mosquito from susceptible to infected compartment
μ_h	Natural death rate of humans
μ_v	Natural death rate of mosquitoes
δ_h	Death rate of humans due to malaria
r	Transfer rate of humans from infected to treated compartment
ε	Transfer rate of humans from treated to recovered compartment
τ	Transfer rate of humans from infected to recovered compartment
φ	Transfer rate of humans from recovered to susceptible compartment
γ	Fraction of natural birth rate of humans.
$(1-\gamma)\psi$	Rate at which newly born humans enter into susceptible compartment
$\gamma\psi$	Rate at which newly born humans enter into protected compartment
g	Transfer rate of humans from susceptible to protected compartment
υ	Vaccination rate on humans
k	Rate at which mosquitoes are killed
ϕ	Rate at which susceptible mosquitoes bite infected humans. (Infected mosquito also bites susceptible humans at the same rate)

Table 2: Variables and description

Variables	Description
$S_h(t)$	the number of susceptible human host at time t
$P_h(t)$	the number of protected human host at time t
$I_h(t)$	the number of infected human host at time t
$T_h(t)$	the number of treated human host at time t
$R_h(t)$	the number of recovered human host at time t
$S_m(t)$	the number of susceptible mosquito vector at time t
$I_m(t)$	the number of infected mosquito vector at time t
$N_h(t)$	the total human population at time t
$N_m(t)$	the total mosquito population at time t

Model formulation

The model by Fekadu*et al.* (2015) is given as

$$\frac{dS_h}{dt} = (1-\gamma)\psi - \frac{\theta_{mh}\phi I_m}{N_h}S_h - \mu_h S_h - gS_h + \varphi R_h \quad (1)$$

$$\frac{dP_h}{dt} = \gamma\psi + gS_h + (1-\varphi)R_h - \mu_h P_h \quad (2)$$

$$\frac{dI_h}{dt} = \frac{\theta_{mh}\phi I_m}{N_h} - \tau I_h - rI_h - \mu_h I_h - \delta_h I_h \quad (3)$$

$$\frac{dT_h}{dt} = rI_h - \varepsilon T_h - \mu_h T_h \quad (4)$$

$$\frac{dR_h}{dt} = \varepsilon T_h + \tau I_h - (1-\varphi)R_h - \varphi R_h - \mu_h R_h \quad (5)$$

$$\frac{dS_m}{dt} = \rho - \frac{\theta_{hm}\phi I_h}{N_h}S_m - \mu_m S_m \quad (6)$$

$$\frac{dI_m}{dt} = \frac{\theta_{hm}\phi I_h}{N_h}S_m - \mu_m I_m \quad (7)$$

Proposed model

We assumed that susceptible and infected mosquitoes are killed at same rate by humans and the inclusion of a vaccination parameter gives the modified model below;

$$\frac{dS_h}{dt} = (1-\gamma)\psi - \frac{\theta_{mh}\phi I_m}{N_h}S_h - \mu_h S_h - gS_h + \varphi R_h - \upsilon S_h \quad (8)$$

$$\frac{dP_h}{dt} = \gamma\psi + gS_h + (1-\varphi)R_h - \mu_h P_h + \upsilon S_h \quad (9)$$

$$\frac{dI_h}{dt} = \frac{\theta_{mh}\phi I_m}{N_h} - \tau I_h - rI_h - \mu_h I_h - \delta_h I_h \quad (10)$$

$$\frac{dT_h}{dt} = rI_h - \varepsilon T_h - \mu_h T_h \quad (11)$$

$$\frac{dR_h}{dt} = \varepsilon T_h + \tau I_h - (1-\varphi)R_h - \varphi R_h - \mu_h R_h \quad (12)$$

$$\frac{dS_m}{dt} = \rho - \frac{\theta_{hm}\phi I_h}{N_h}S_m - \mu_m S_m - kS_m \quad (13)$$

$$\frac{dI_m}{dt} = \frac{\theta_{hm}\phi I_h}{N_h}S_m - \mu_m I_m - kI_m \quad (14)$$

Analysis of the Model

The total population sizes N_h and N_m can be determined by $S_h + P_h + I_h + T_h + R_h = N_h$ and $S_m + I_m = N_m$. The initial conditions of the system of equations (8) - (14) are given by $S_h(0) = S_{h0}$, $P_h(0) = P_{h0}$, $I_h(0) = I_{h0}$, $T_h(0) = T_{h0}$, $R_h(0) = R_{h0}$, $S_m(0) = S_{m0}$, $I_m(0) = I_{m0}$. Considering the total human population, we have $\frac{dN_h}{dt} = \psi - \mu_h N_h - \delta_h I_h$. When the term $\delta_h I_h$ vanishes in equation (8) - (14), we obtain the solution of $\frac{dN_h}{dt} = \psi - \mu_h N_h$ to be $N_h(t) = \frac{\psi}{\mu_h} + [N_{h0} - (\psi/\mu_h)]e^{-\mu_h t}$ showing that $N_h(t) \to \frac{\psi}{\mu_h}$ as $t \to 0$. Similarly, on summing up the total mosquito population, we have

$\frac{dN_m}{dt} = \rho - N_m(\mu_m + k)$ which yields the solution, $N_m(t) = \frac{\rho}{\mu_m} + [N_{m0} - [\rho/(\mu_m + k)]]e^{-\mu_m t}$ showing that $N_m(t) \to \frac{\rho}{(\mu_m + k)}$ as $t \to 0$.

Disease free equilibrium point

The disease free equilibrium point, denoted by $E_o = (S_h^*, P_h^*, I_h^*, T_h^*, R_h^*, S_m^*, I_m^*)$, are steady state solutions in the absence of the disease in human and the parasite in the mosquito population. By setting the right-hand side of equations (8) - (14) to zero and then evaluating, yields the equilibrium point,

$$E_o = \left(\frac{\psi(1-\gamma)}{\mu_h + g + \upsilon}, \frac{\psi(\upsilon + g + \gamma\mu_h)}{\mu_h(\mu_h + g + \upsilon)}, 0, 0, 0, \frac{\rho}{(\mu_m + k)}, 0\right).$$

Basic reproduction number R_o

This is the threshold quantity for many epidemiological models. It determines when and whether a disease will die out in a population or become an epidemic. The threshold quantity indicates the number of secondary infections produced by a single primary infection in a completely susceptible population (Hethcote, 2000). When R_o < 1, each infected individual averagely produces less than one new infected individual and as such, the disease dies out completely over time. On the other hand, if R_o >1, each infected individual averagely produces more than one infected individual so that the disease spread and grow in the population, thus resulting in an epidemic. In the computation of R_o, using the next generation matrix, it is relevant to distinguish new infections from all other changes in the population. We identify I_h and I_m as the relevant classes for the computation of R_o. An infectious event increases these classes (gain terms) and loses from these classes means loss of current or future infectious individual (loss terms). Listing the gain and loss terms (Table 3) for each class and creating a matrix (F) of gain terms and matrix (V) of loss terms with each evaluated at E_o, we have

Table 3: Grouping of gains and loss terms in the infectious compartment for human and mosquito population

Classes	I_h	I_m
Gains	$\theta_{mh}\phi I_m S_h$	$\theta_{hm}\phi I_h S_m$
Losses	$[\tau + r + (\mu_h + \delta_h)I_h]$	$(\mu_m + k)I_m$

$$F = \begin{bmatrix} \frac{\partial}{\partial I_h}\left(\frac{\theta_{mh}\phi I_m S_h}{N_h}\right) & \frac{\partial}{\partial I_h}\left(\frac{\theta_{hm}\phi I_h S_m}{N_h}\right) \\ \frac{\partial}{\partial I_m}\left(\frac{\theta_{mh}\phi I_m S_h}{N_h}\right) & \frac{\partial}{\partial I_m}\left(\frac{\theta_{hm}\phi I_h S_m}{N_h}\right) \end{bmatrix}_{E_o} = \begin{bmatrix} 0 & \frac{\theta_{mh}\phi}{N_h}\left(\frac{\rho}{\mu_m + k}\right) \\ \frac{\theta_{mh}\phi}{N_h}\left(\frac{\psi(1-\gamma)}{\mu_h + g + \upsilon}\right) & 0 \end{bmatrix}$$

Similarly;

$$V = \begin{bmatrix} \frac{\partial}{\partial I_h}[\tau + r + (\mu_h + \delta_h)]I_h & \frac{\partial}{\partial I_h}(\mu_m + k)I_m \\ \frac{\partial}{\partial I_m}[\tau + r + (\mu_h + \delta_h)]I_h & \frac{\partial}{\partial I_m}(\mu_m + k)I_m \end{bmatrix}_{E_o} = \begin{bmatrix} \tau + r + (\mu_h + \delta_h) & 0 \\ 0 & \mu_m + k \end{bmatrix}$$

Taking the inverse of V yields

$$V^{-1} = \begin{bmatrix} \frac{1}{\tau + r + (\mu_h + \delta_h)} & 0 \\ 0 & \frac{1}{(\mu_m + k)} \end{bmatrix}$$ and evaluating $G = FV^{-1}$ gives

$$G = \begin{bmatrix} 0 & \frac{\rho\theta_{hm}\phi}{N_h(\mu_m + k)^2} \\ \frac{\psi(1-\gamma)\theta_{mh}\phi}{N_h(\mu_h + g + \upsilon)[\tau + r + (\mu_h + \delta_h)]} & 0 \end{bmatrix}.$$

R_o is the dormant eigenvalue, $\lambda_{\max}$ of G, with $\lambda_{\max} = \frac{T}{2} + \sqrt{\left(\frac{T^2}{2}\right) - D}$ where T and D are the trace and determinant of matrix G. Since $T = 0$, therefore

$$R_o = \lambda_{\max} = \sqrt{-D} = \sqrt{\frac{(1-\gamma)\theta_{mh}\theta_{hm}\phi^2\rho\mu_h^2}{\psi(\mu_m + k)^2(\mu_h + g + \upsilon)[\tau + r + (\mu_h + \delta_h)]}}. \quad (15)$$

Stability of the disease free equilibrium point

To establish the disease free equilibrium, the Jacobian matrix of equation (8) - (14) is computed and evaluated at E_o, thus yielding;

$$J_{E_o} = \begin{pmatrix} -Q & 0 & 0 & 0 & \varphi & 0 & -\left(\frac{\theta_{mh}\phi\psi(1-\gamma)}{N_h Q}\right) \\ g+\upsilon & -\mu_h & 0 & 0 & 1-\varphi & 0 & 0 \\ 0 & 0 & -M & 0 & 0 & 0 & \left(\frac{\theta_{mh}\phi\psi(1-\gamma)}{N_h Q}\right) \\ 0 & 0 & r & -(\varepsilon+\mu_h) & 0 & 0 & 0 \\ 0 & 0 & \tau & \varepsilon & -(1+\mu_h) & 0 & 0 \\ 0 & 0 & -\left(\frac{\theta_{hm}\phi\rho}{N_h L}\right) & 0 & 0 & -L & 0 \\ 0 & 0 & \left(\frac{\theta_{hm}\phi\rho}{N_h L}\right) & 0 & 0 & 0 & -L \end{pmatrix},$$

Where: $Q = (\mu_h + g + \upsilon)$, $M = (\tau + r + \mu_h + \delta_h)$ and $L = (\mu_m + k)$.

To get the eigenvalues, we obtain the characteristic equation.

Thus,

$$\left|J_{E_o} - \lambda I\right| = \begin{vmatrix} -Q-\lambda & 0 & 0 & 0 & \varphi & 0 & -\left(\frac{\theta_{mh}\phi\psi(1-\gamma)}{N_h Q}\right) \\ g+\upsilon & -\mu_h-\lambda & 0 & 0 & 1-\varphi & 0 & 0 \\ 0 & 0 & -M-\lambda & 0 & 0 & 0 & \left(\frac{\theta_{mh}\phi\psi(1-\gamma)}{N_h Q}\right) \\ 0 & 0 & r & -(\varepsilon+\mu_h)-\lambda & 0 & 0 & 0 \\ 0 & 0 & \tau & \varepsilon & -(1+\mu_h)-\lambda & 0 & 0 \\ 0 & 0 & -\left(\frac{\theta_{hm}\phi\rho}{N_h L}\right) & 0 & 0 & -L-\lambda & 0 \\ 0 & 0 & \left(\frac{\theta_{hm}\phi\rho}{N_h L}\right) & 0 & 0 & 0 & -L-\lambda \end{vmatrix}$$

$$= [-\mu_h - \lambda][-Q-\lambda][-(\varepsilon+\mu_h)-\lambda][-(1+\mu_h)-\lambda][-L-\lambda]\begin{vmatrix} -M-\lambda & \left(\frac{\theta_{mh}\phi\psi(1-\gamma)}{N_h Q}\right) \\ \left(\frac{\theta_{hm}\phi\rho}{N_h L}\right) & -L-\lambda \end{vmatrix} = 0$$

$$= [-\mu_h - \lambda][-Q-\lambda][-(\varepsilon+\mu_h)-\lambda][-(1+\mu_h)-\lambda][-L-\lambda]\left[\begin{matrix} \lambda^2 + [M+L]\lambda + ML - \\ \frac{\theta_{mh}\theta_{hm}\phi^2\rho\psi(1-\gamma)}{N_h^2 LQ} \end{matrix}\right] = 0$$

so the eigenvalues of the characteristic equation are then given by

$$[-\mu_h],[-Q],[-(\varepsilon+\mu_h)],[-(1+\mu_h)],[-L],\frac{-[M+L]\pm\sqrt{[M+L]^2-4\left[ML-\dfrac{\theta_{mh}\theta_{hm}\phi^2\rho\psi(1-\gamma)}{N_h^2LQ}\right]}}{2}.$$

And from equation (15), we have the eigenvalues in terms of R_o to be

$$[-\mu_h],[-Q],[-(\varepsilon+\mu_h)],[-(1+\mu_h)],[-L],\frac{-[M+L]\pm\sqrt{[M+L]^2-4ML[1-R_o]}.}{2}$$

Thus, we obtain;

$$R_o=\frac{\left[\dfrac{\theta_{mh}\theta_{hm}\phi^2\rho\psi(1-\gamma)}{N_h^2LQ}\right]}{ML}=\frac{1}{ML}\left[\frac{\theta_{mh}\theta_{hm}\phi^2\rho\psi(1-\gamma)}{N_h^2LQ}\right]$$ and by substituting the expressions for M, N_h, L and Q yields $R_o=\dfrac{(1-\gamma)\theta_{mh}\theta_{hm}\phi^2\rho\mu_h^2}{\psi(\mu_m+k)^2(\mu_h+g+\upsilon)[\tau+r+(\mu_h+\delta_h)]}$ which conforms to the solution in equation (15) obtained based on the next generation matrix method.

The eigenvalues are hereby analyzed below;

$\lambda_1=-\mu_h<0$, $\lambda_2=-Q=-(\mu_h+g+\upsilon)<0$, $\lambda_3=-(\varepsilon+\mu_h)<0$, $\lambda_4=-(1+\mu_h)<0$, $\lambda_5=-L=-(\mu_m+k)<0$.

$$\lambda_6=\frac{-[M+L]+\sqrt{[M+L]^2-4ML[1-R_o]}}{2}$$

$$\lambda_7=\frac{-[M+L]-\sqrt{[M+L]^2-4ML[1-R_o]}}{2}$$

If $1-R_o>0$, then $R_o<1$ and

$$\lambda_6<\frac{-[M+L]}{2}+\frac{\sqrt{[M+L]^2}}{2}=0,\text{ and}$$

$$\lambda_7<\frac{-[M+L]}{2}-\frac{\sqrt{[M+L]^2}}{2}=-[M+L]=-[(\tau+r+\mu_h+\delta_h)+(\mu_m+k)]$$

Therefore, $\lambda_6<0$ and $\lambda_7<0$ thus establishing $\lambda_1<0$, $\lambda_2<0$, $\lambda_3<0$, $\lambda_4<0$, $\lambda_5<0$, $\lambda_6<0$, $\lambda_7<0$

Theorem

Given the system of equations in (8) - (14) and that $\gamma,\psi,\varphi,\tau,\upsilon,r,g,\mu_h,\mu_m,k,\varepsilon,\delta>0$, the disease-free equilibrium E_o is locally asymptotically stable if and only if, $R_o\leq 1$, (Li *et al.*,1999).

Discussion

The Fekadu*et al*. (2015) SPITR mathematical model was modified by including parameters for vaccination, vector-population reduction for the dynamics of malaria within human host and mosquito vectors. The model was analyzed in terms of actual population. The stability of the equilibrium point obtained by method of linearization were analyzed and found to be locally asymptotically stable. The effect of vaccination alone on the susceptible human class of the modified SPITR host modelreduces the number of susceptible human population against possible infection or re-infection, thus in the long run reduces the number of infectious human population. A combination of vector-population reduction, treatment, as well as vaccination of susceptible human, aimed at prevention, clearly indicates that malaria can be eliminated in the shortest possible time.

Conclusion

In consideration of the findings of this study as well as the incidental observations, to be able to eradicate malaria in the population, we recommend that a reasonable level of the combination of treatment, vaccination and vector-mosquito reduction should be maintained.

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