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Research article

Vaccination and combined optimal control measures for malaria prevention and spread mitigation

Khadiza Akter Eme[1], **Md Kamrujjaman**[2,3,*], **Muntasir Alam**[4] **and Md Afsar Ali**[5]

[1] Department of Physical Sciences, Independent University, Bangladesh, Dhaka 1229, Bangladesh
[2] Department of Mathematics, University of Dhaka, Dhaka 1000, Bangladesh
[3] Department of Mathematics, Asian University for Women, Chittagong 4000, Bangladesh
[4] Department of Applied Mathematics, University of Dhaka, Dhaka 1000, Bangladesh
[5] Department of Mathematics, Tuskegee University, Tuskegee, AL 36088, USA

* **Correspondence:** Email: kamrujjaman@du.ac.bd.

Supplementary

1. Auxiliary results

The Susceptible-Vaccinated-Infected-Removal-Susceptible (SVIRS) model is a widely used framework for predicting infectious disease dynamics. In this study, we adapt and extend this approach to develop a mathematical model specifically tailored for malaria. The model that we have used in our study is read as follows:

$$\begin{cases} S'_h(t) = \tau_1 - \beta \frac{S_h I_m}{N} + \rho R_h - (\omega + \mu) S_h, \\ V'_h(t) = \omega S_h - 0.7 * \beta \frac{V_h I_m}{N} - (\mu + \gamma_1) V_h, \\ I'_h(t) = \beta \frac{S_h I_m}{N} + 0.7 * \beta \frac{V_h I_m}{N} - (\gamma_2 + \delta + \mu) I_h, \\ R'_h(t) = \gamma_1 V_h + \gamma_2 I_h - (\rho + \mu) R_h, \\ S_m{}'(t) = \tau_2 - \alpha \frac{S_m I_h}{N} - \eta S_m, \\ I_m{}'(t) = \alpha \frac{S_m I_h}{N} - \eta I_m \end{cases} \tag{1.1}$$

for $t \in [0, \infty)$ with initial conditions

$$S_h(0) = S_{h0},\ V_h(0) = V_{h0},\ I_h(0) = I_{h0},\ R_h(0) = R_{h0},\ S_m(0) = S_{m0},\ I_m(0) = I_{m0}. \tag{1.2}$$

In this section, we have presented the theoretical results to ensure the existence and uniqueness theorem, find out the disease-free equilibrium (DFE), endemic equilibrium (EE) and determine the basic reproduction number (R_0), and establish other auxiliary results.

1.1. Positivity and boundedness of solutions

Theorem 1. *The closed region* $\Omega = \{(S_h, V_h, I_h, R_h, S_m, I_m) \in \mathbb{R}^6_+ : 0 < N \leq \frac{\tau_1}{\mu}, 0 < M \leq \frac{\tau_2}{\eta}\}$ *is positively invariant set for the system in Eq* (1.1).

Proof. Since

$$N(t) = S_h(t) + V_h(t) + I_h(t) + R_h(t)$$

then

$$\begin{aligned}\frac{dN}{dt} =& \frac{dS_h}{dt} + \frac{dV_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt}\\ =& \tau_1 - \mu(S_h + V_h + I_h + R_h) - \delta I_h\\ =& \tau_1 - \mu N - \delta I_h\end{aligned}$$

This implies

$$\frac{dN}{dt} \leq \tau_1 - \mu N. \tag{1.3}$$

Hence, $\frac{dN}{dt} < 0$ whenever

$$\frac{\tau_1}{\mu} < N(t).$$

It shows that $\frac{dN}{dt}$ is bounded by $\frac{\tau_1}{\mu}$.
Now, integrating the inequality in (1.3) and using the initial condition, we obtain

$$N(t) \leq N(0)e^{-\mu t} + \frac{\tau_1}{\mu}(1 - e^{-\mu t}). \tag{1.4}$$

Letting, $t \to \infty$, we get $N(t) \leq \frac{\tau_1}{\mu}$ asymptotically.
Similarly, we can show that $t \to \infty$, $M(t) \leq \frac{\tau_2}{\eta}$ asymptotically. Therefore, Ω is positively invariant set of the model (1.1) so that no solution path leaves through the boundary of Ω. This completes the proof that the formulated model is relevant both mathematically and epidemiologically.

1.2. Steady states

We rewrite (1.1) as follows:

$$\begin{cases} S'_h(t) = \tau_1 - \beta\frac{S_h I_m}{N} + \rho R_h - k_1 S_h,\\ V'_h(t) = \omega S_h - 0.7\beta\frac{V_h I_m}{N} - k_2 V_h,\\ I'_h(t) = \beta\frac{S_h I_m}{N} + 0.7\beta\frac{V_h I_m}{N} - k_3 I_h,\\ R'_h(t) = \gamma_1 V_h + \gamma_2 I_h - k_4 R_h,\\ S_m{\prime}(t) = \tau_2 - \alpha\frac{S_m I_h}{N} - \eta S_m,\\ I_m{\prime}(t) = \alpha\frac{S_m I_h}{N} - \eta I_m \end{cases} \tag{1.5}$$

where $k_1 = (\omega + \mu)$, $k_2 = (\mu + \gamma_1)$, $k_3 = (\gamma_2 + \delta + \mu)$, $k_4 = (\rho + \mu)$

Disease-free equilibrium (DFE)

For computing the equilibrium points of our system, let us assume all the time derivatives equal to zero. After setting zero to all of the time derivatives,we get

$$\begin{cases} \tau_1 - \beta\frac{S_h I_m}{N} + \rho R_h - k_1 S_h = 0, \\ \omega S_h - 0.7\beta\frac{V_h I_m}{N} - k_2 V_h = 0, \\ \beta\frac{S_h I_m}{N} + 0.7\beta\frac{V_h I_m}{N} - k_3 I_h = 0, \\ \gamma_1 V_h + \gamma_2 I_h - k_4 R_h = 0, \\ \tau_2 - \alpha\frac{S_m I_h}{N} - \eta S_m = 0, \\ \alpha\frac{S_m I_h}{N} - \eta I_m = 0. \end{cases} \tag{1.6}$$

At DFE $I_h = 0$, and $I_m = 0$ as we have supposed that there exists no infection at the DFE point. After that, by solving the system (1.6), we get the disease-free equilibrium. We denote it by $P_0 \equiv (S_{h0}, V_{h0}, I_{h0}, R_{h0}, S_{m0}, I_{m0})$ where

$$S_{h0} = k_2 k_4 k, V_{h0} = \omega k_4 k, I_{h0} = 0, R_{h0} = \omega\gamma_1 k, S_{m0} = \frac{\tau_2}{\eta}, I_{m0} = 0,$$

where $k = \dfrac{\tau_1}{k_1 k_2 k_4 - \gamma_1 \rho\omega}$.

Basic reproduction number

The basic reproduction number is an important threshold for studying infectious illness models. It indicates if the illness will disappear or persist in the population. The basic reproduction number, $\mathcal{R}_0$, 'the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual'. If $\mathcal{R}_0 > 1$, the DFE is unstable, that indicates a single primary illness might cause multiple secondary infections, resulting in an epidemic. If $\mathcal{R}_0 < 1$, the DFE is locally asymptotically stable, which means that the illness will not survive in the community, as a result, the state will be sustainable.

The basic reproduction number of the system (1.1) will be obtained by the next generation matrix method. For this we will use the system (1.5). We obtain two following matrix from the system (1.5) which are F and V, they are given as

$$F = \begin{pmatrix} 0 & \dfrac{\beta}{N}(S_{h0} + 0.7V_{h0}) \\ \dfrac{\alpha S_{m0}}{N} & 0 \end{pmatrix} = \begin{pmatrix} 0 & \dfrac{\beta}{N}(k_2 k_4 k + 0.7 w k_4 k) \\ \dfrac{\alpha\tau_2}{\eta N} & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} k_3 & 0 \\ 0 & \eta \end{pmatrix}.$$

Therefore, the V^{-1} matrix is

$$V^{-1} = \begin{pmatrix} \dfrac{1}{\eta} & 0 \\ 0 & \dfrac{1}{k_3} \end{pmatrix}$$

Thus, FV^{-1}, that is, the next-generation matrix is

$$FV^{-1} = \begin{pmatrix} 0 & \dfrac{\beta k_4 k(k_2 + 0.7\omega)}{N} \\ \dfrac{\alpha\tau_2}{\eta k_3 N} & 0 \end{pmatrix}.$$

Therefore,

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\sqrt{\alpha\beta\tau_2 k_4 k(0.7\omega + k_2)}}{N\eta\sqrt{k_3}}.$$

Endemic equilibrium (EE)

For the endemic equilibrium (EE), we replace the variables as $(S_h, V_h, I_h, R_h, S_m, I_m) \equiv (S_h^*, V_h^*, I_h^*, R_h^*, S_m^*, I_m^*)$, where, $I_h^* > 0$ and $I_m^* > 0$. And we get the system as follows

$$\begin{cases} \tau_1 - \beta\frac{S_h^* I_m^*}{N} + \rho R_h^* - k_1 S_h^* = 0, \\ \omega S_h - 0.7\beta\frac{V_h^* I_m^*}{N} - k_2 V_h^* = 0, \\ \beta\frac{S_h^* I_m^*}{N} + 0.7\beta\frac{V_h^* I_m^*}{N} - k_3 I_h^* = 0, \\ \gamma_1 V_h^* + \gamma_2 I_h^* - k_4 R_h^* = 0, \\ \tau_2 - \alpha\frac{S_m^* I_h^*}{N} - \eta S_m^* = 0, \\ \alpha\frac{S_m^* I_h^*}{N} - \eta I_m^* = 0. \end{cases}$$

Solving this system, we get the EE as $(S_h^*, V_h^*, I_h^*, R_h^*, S_m^*, I_m^*)$ where

$$\begin{cases} S_h^* = \dfrac{(a_6 + a_7 I_h^*)(b_4 + b_7 I_h^*)}{(a_3 + a_{10} I_h^*)(b_4 + b_7 I_h^*) - a_{11}(b_1 + b_2) I_h^{*2}}; \\ V_h^* = \dfrac{(a_6 + a_7 I_h^*)(b_1 + b_2 I_h^*)}{(a_3 + a_{10} I_h^*)(b_4 + b_7 I_h^*) - a_{11}(b_1 + b_2) I_h^{*2}}; \\ R_h^* = \dfrac{\gamma_1 (a_6 + a_7 I_h^*)(b_1 + b_2 I_h^*)}{a_1((a_3 + a_{10} I_h^*)(b_4 + b_7 I_h^*)^2 - a_{11}(b_1 + b_2)(b_4 + b_7 I_h^*) I_h^{*2})} + \dfrac{\gamma_2 I_h^*}{a_1}; \end{cases}$$

$$\begin{cases} S_m^* = \dfrac{N\tau_2}{\alpha I_h^* + N\eta}; \\ I_m^* = \dfrac{\alpha\tau_2 I_h^*}{\eta(\alpha I_h^* + N\eta)}; \\ I_h^* = \dfrac{f_1}{f_2 \pm (f_5 + f_3\sqrt{f_4})}; \end{cases}$$

where,
$a_1 = \rho + \mu$; $a_2 = \omega + \mu$; $a_3 = a_1 a_2 \eta^2 N^3$; $a_4 = a_1 a_2 \alpha\eta N^2$; $a_5 = a_1 \alpha\beta\tau_2 N$; $a_6 = a_1 \tau_1 \eta^2 N^3$;
$a_7 = a_1 \tau_1 \eta\alpha N^2$; $a_8 = \rho\gamma_1 \eta^2 N^3$; $a_9 = \rho\gamma_1 \eta\alpha N^2$; $a_{10} = a_4 + a_5$; $a_{11} = a_8 + a_9$;
$b_1 = \omega\eta^2 N^2$; $b_2 = \alpha\omega\eta N$; $b_3 = \mu + \gamma_1$; $b_4 = b_3 \eta^2 N^2$; $b_5 = b_3 \alpha\eta N$; $b_6 = 0.7\beta\tau_2$; $b_7 = b_5 + b_6$;
$c_1 = n\eta$;

$c_2 = \alpha\beta\tau_2;$
$c_3 = \alpha\eta\tau_1 k_4 + c_1\eta k_3 k_4 - c_1\eta\gamma_2\rho;$
$c_4 = 100k_2 + 140\omega + 49\omega^2;$
$c_5 = k_3 k_4;$
$c_6 = 140k_1k_2 - 98k_1\omega - 200k_2^2 - 140k_2\omega;$
$c_7 = \rho\gamma_2 - \alpha\tau_1 k_4 - c_5;$
$c_8 = 49k_1^2 - 140k_1k_2 + 100k_2^2;$
$c_9 = 200k_2^2 + 280k_2\omega + 98\omega^2;$
$c_{10} = -140k_1k_2 + 98k_1\omega + 200k_2^2 + 140k_2\omega;$
$c_{11} = 100k_2^2 + 140k_2\omega + 49\omega^2;$
$c_{12} = -140k_2 - 98\omega - 98k_1 + 140k_2k_3 + 196k_3\omega;$
$c_{13} = 140k_2 + 98\omega;$
$c_{14} = 7\rho^2 k_1 + 10\eta^2 k_2;$
$c_{15} = \rho\gamma_2 - \alpha k_4\tau_1 - c_5;$
$d_1 = k_3k_4 - \gamma_2\rho;$
$d_2 = k_1k_4 - \gamma_1\rho\omega;$
$d_3 = k_1k_3k_4 - \gamma_2\rho\omega;$
$d_4 = \gamma_1\rho\omega - k_1k_2k_4;$
$d_5 = 10k_2 + 7\omega;$
$d_6 = \alpha\tau_1 + Nk_3\eta;$
$d_7 = 7k_1 + 10k_2;$
$d_8 = 10k_2\rho + 7\beta\omega;$
$d_9 = N\beta\eta\tau_2;$
$f_1 = (10c_1^3k_3d_4 + \alpha\tau_1k_4d_5d_9)(2\alpha\beta\eta k_4d_6 - d_9\eta\rho)(7\beta^2 tau_2^2 d_1 - 10d_4c_1^2k_3 + c_5d_7d_9 - \gamma_2d_8d_9);$
$f_2 = 7\beta\tau_1c_2d_1 + 10\alpha c_1^2 d_2 + 7c_2c_1d_3 + 10c_1c_2k_2d_1;$
$f_3 = \beta^2\tau_2c_3;$
$f_4 = c_1^4c_4k_2\gamma_1^2 + c_1^4\gamma_2\rho c_5c_6 - 280c_1^3\rho\gamma_1\omega k_3c_{15} + c_1^4c_5^2c_8c_1^3c_9 + c_1^3c_5\alpha k_4\tau_1c_{10} + c_1^2\alpha^2k_4^2\tau_1^2c_{11} + c_1^2c_2\gamma_2\rho\tau_1k_2k_4 + c_1c_2\alpha\tau_1^2k_4^2c_{13} + 49c_2^2k_4^2\tau_1^2;$
$f_5 = c_1^2\gamma_2\rho d_5 + c_1\alpha\tau_1k_4d_5 - N^2c_5c_{14} - 7\tau_1k_1c_2;$

Hence the endemic steady state is completely depending on I_h^*.

Theorem 2. *For system (1.5), the DFE P_0 is locally asymptotically stable if $R_0 < 1$.*

Proof. The Jacobian matrix of the system (1.5) at DFE is

$$J_0 = \begin{pmatrix} -k_1 & 0 & 0 & \rho & 0 & -\dfrac{\beta k_2 k_4 k}{N} \\ \omega & -k_2 & 0 & 0 & 0 & -\dfrac{0.7\beta\omega k_4 k}{N} \\ 0 & 0 & -k_3 & 0 & 0 & \dfrac{\beta k_4 k(k_2 + 0.7\omega)}{N} \\ 0 & \gamma_1 & \gamma_2 & -k_4 & 0 & 0 \\ 0 & 0 & -\dfrac{\alpha\tau_2}{\eta N} & 0 & -\eta & 0 \\ 0 & 0 & \dfrac{\alpha\tau_2}{\eta N} & 0 & 0 & -\eta \end{pmatrix}.$$

Then the characteristic equation is

$$(\lambda + \eta)(a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4)(a_5\lambda^2 + a_6\lambda + a_7) = 0 \tag{1.7}$$

where $a_1 = 1 > 0$;
$a_2 = k_1 + k_2 + k_4 > 0$;
$a_3 = k_1k_2 + k_1k_4 + k_2k_4 > 0$;
$a_4 = k_1k_2k_4 - \gamma_1\rho\omega = \mu^3 + \mu^2(\rho + \omega + \gamma_1) + \mu(\rho\omega + \rho\gamma_1 + \omega\gamma_1) > 0$;
$a_5 = \eta N^2 > 0$;
$a_6 = \eta^2N^2 + k_3\eta N^2 > 0$;
$a_7 = k_3\eta^2N^2 - \alpha\beta\tau_2kk_2k_4 - 0.7\alpha\beta\tau_2\omega kk_4 = k_3\eta^2N^2 - \alpha\beta\tau_2kk_4(k_2 + 0.7\omega) = k_3\eta^2N^2(1 - R_0^2) > 0$
$if R_0 < 1$.
From the above characteristic equation, one of the eigenvalues is -η which is clearly negative and three other eigenvalues are the roots of the following cubic equation

$$a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0,$$

where, $a_i > 0, i = 1, 2, 3, 4$ and $a_2a_3 > a_4$. So, by the Routh - Hurwitz criterion, all roots of the above cubic equation have negative real part. The solutions of the following quadratic equation gives the other two eigenvalues.

$$a_5\lambda^2 + a_6\lambda + a_7 = 0,$$

where, $a_i > 0, i = 5, 6$ and $a_7 > 0$ if $R_0 < 1$. Then, by the Routh - Hurwitz criterion, all roots of the quadratic equation have negative real part. Thus, for $R_0 < 1$, all roots of (1.7) have negative real parts. This completes the proof.