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MATHEMATICAL ANALYSIS FOR DYNAMICAL SPREAD OF MALARIA IN THE POPULATION WITH CONTROLLING MEASURES

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ABSTRACT: A system of differential equation approach was used to model the dynamical spread of malaria where humans and vectors interact and infect each other. Positivity of solution showed that there exists a domain where the model is epidemiologically and mathematically well-posed. The basic reproduction number $R_0 < 1$ shows that disease can be controlled in the environment, otherwise the disease persist and become endemic whenever $R_0 > 1$. Also, the numerical analysis performed shows that the most effective strategies for controlling malaria is to reduce the vector biting rate and increased the human treatment.

KEYWORDS: Malaria, Humans, vectors, mathematical model, stability analysis, simulation study.

1 INTRODUCTION

Malaria is one of deadliest infectious disease caused by a parasite that lives part of its life in humans and the remaining in vectors. Malaria is a major killer of humans worldwide, claiming the lives of millions of people around the world. Malaria is widely spreads in the tropical areas of Asia, Africa, and Central and South America, where it affects millions of people. Each year, about 350 to 500 million cases of malaria recorded globally. However, more than one million of its victims, mostly young children, die yearly, although, malaria has been virtually eradicated in the United States and other regions with temperate climates [22].

Malaria is caused by a single-celled parasite from the genus Plasmodium, different species of Plasmodium exist. They produce malaria in various types of animals and birds, as well as in humans. Four of these species of Plasmodium commonly infect humans. Each one has a different appearance under the microscope, and each one produces a somewhat different pattern of symptoms. More than two species can live in the same area and infect a single person at the same time. Plasmodium falciparum is responsible for most malaria deaths, especially in Africa. Suddenly, the infection can develop and produce several life-threatening complications. With prompt and effective treatment, however, it is almost always curable.

Malaria parasite is transmitted to people through genus Anopheles mosquitoes. In rare cases, a person may become infected through contaminated blood, or a fetus may become infected by its mother during pregnancy, or after delivery. Also, because the malaria parasite is found in RBCs, malaria can also be transmitted through the unscreened, blood transfusion, organ transplant, or the shared use of needles or syringes contaminated with blood. Many biological and environmental factors shape the character of malaria in a given location, nearly all the people who live in endemic areas are exposed to infection repeatedly. Those who survive malaria in childhood gradually build up some immunity. They may carry the infection, serving as a mode of transmission by vectors without developing severe disease, [25].

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Having gone through the work of many researchers on mathematical modeling of malaria, but precisely the work of [11] by incorporating the treated human and exposed vector

In this paper, we developed a mathematical model in order to assess the potential impact of biting rate and treatment strategies on the dynamics spread of malaria taking both host and vector populations into account.

2 MATHEMATICAL FORMULATION

A system of differential equations are introduced to model the dynamical spread of malaria with control in two interacting population of humans and vector, we divided the total human population $N_h(t)$, into Susceptible humans $S_h(t)$, Exposed humans $E_h(t)$, Infectious humans $I_h(t)$, Treated humans $T_h(t)$ and Recovered- humans $R_h(t)$

i.e. $N_h(t) = S_h(t) + E_h(t) + I_h(t) + T_h(t) + R_h(t)$. (2.1)

Unlike human population, we divided the vector population into three subclasses: Susceptible vector $S_v(t)$, Exposed vector $E_v(t)$ and Infectious vector $I_v(t)$ .The vector remain infectious for life and have no recovered class. Thus, the total size of the vector population at any time (t) is denoted by

$$N_v(t) = S_v(t) + E_v(t) + I_v(t) \quad (2.2)$$

The population of susceptible humans is increased through recruitment of humans (by birth or immigration) into the society at rate π_h and by recovered human at rate ψ due to waning of immunity acquired after successful treatment. It is decreased by infection acquired through bite with infected vector at rate α_h and natural death at rate μ_h.

This gives: $\frac{dS_h}{dt} = \pi_h + \psi R_h - \alpha_h S_h - \mu_h S_h$ (2.3)

An exposed human is generated through infection of susceptible at rate α_h . It reduces due to progression of human from exposed to infectious at rate κ_h and natural death at rate μ_h. Thus $\frac{dE_h}{dt} = \alpha_h S_h - \kappa_h E_h - \mu_h E_h$ (2.4)

Infected human is generated through progression of humans exposed to vector at rate κ_h. It diminishes due to recovery at rate r , natural death at rate μ_h, vector induced death rate δ and treatment of infection human at rate τ. Therefore

$$\frac{dI_h}{dt} = \kappa_h E_h - rI_h - (\mu_h + \delta) I_h - \tau I_h \quad (2.5)$$

The treated human is generated by the treatment of human from infection at rate τ . It reduces through progression from treatment to recovery at rate ε and natural death at rate μ_h. Thus $\frac{dT_h}{dt} = \tau I_h - \varepsilon T_h - \mu_h T_h$ (2.6)

The recovered humans are generated by the recovery of infected human and the progression from treatment to recovery at rate ε . It decreased by loss of immunity at rate ψ and natural death at rate ψ_h. Thus

$$\frac{dR_h}{dt} = rI_h + \varepsilon T_h - \psi R_h - \mu_h R_h \quad (2.7)$$

The susceptible vector is generated through recruitment of vector (by birth or immigration) at rate π_v It reduced by infection, acquired when susceptible vector bite infected humans at rate α_v and by natural death at rate μ_v. This yield

$$\frac{dS_v}{dt} = \pi_v - \alpha_v S_v - \mu_v S_v \quad (2.8)$$

The population of exposed vector is generated through infection of susceptible at rate α_v. It decreased by progression of vector from exposed to infectious at rate κ_v also by natural death at rate μ_v. Thus

$$\frac{dE_v}{dt} = \alpha_v S_v - \kappa_v E_v - \mu_v E \quad (2.9)$$

The infected vector is generated through progression of vector from exposed to infectious class at rate κ_v. It reduced by natural death at rate μ_h. Thus

$$\frac{dI_v}{dt} = \kappa_v E_v - \mu_v I_v \tag{3.0}$$

Equations (2.3) - (2.8) summarize the dynamics of malaria transmission with controlling measures. This lead to the following system of nonlinear ordinary differential equations:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \pi_h + \psi R_h - \alpha_h S_h - \mu_h S_h \\
\frac{dE_h}{dt} &= \alpha_h S_h - \kappa_h E_h - \mu_h E_h \\
\frac{dI_h}{dt} &= \kappa_h E_h - rI_h - (\mu_h + \delta) I_h - \tau I_h \\
\frac{dT_h}{dt} &= \tau I_h - \varepsilon T_h - \mu_h T_h \\
\frac{dR_h}{dt} &= rI_h + \varepsilon T_h - \psi R_h - \mu_h R_h \\
\frac{dS_v}{dt} &= \pi_v - \alpha_v S_v - \mu_v S_v \\
\frac{dE_v}{dt} &= \alpha_v S_v - \kappa_v E_v - \mu_v E_v \\
\frac{dI_v}{dt} &= \kappa_v E_v - \mu_v I_v
\end{aligned}\right\} \tag{3.1}$$

With initial conditions $S_h(0) = S_{h0}, E_h(0) = E_{h0}, I_h(0) = I_{h0}, T_h(0) = T_{h0}, R_h(0) = R_{h0},$
$S_v(0) = S_{v0}, E_v(0) = E_{v0}, I_v(0) = I_{v0}$

where $\alpha_h = \frac{\beta_{vh}\phi I_v}{N_v}$ and $\alpha_v = \frac{\beta_{hv}\phi(E_h + \eta I_h)}{N_h}$ in the model, the term $\frac{\beta_{vh}\phi I_v}{N_v}$ denotes the rate at which the susceptible humans S_h, become infected by infectious female vectors I_v and $\frac{\beta_{hv}\phi(E_h + \eta I_h)}{N_h}$ refers to the rate at which the susceptible vector S_v become infected by infectious humans I_h. It is important to note that the rate of infection of susceptible human S_h by infected vector I_v is dependent on the total number of humans N_h available per vector, [17].

Table 1: Variables and Parameters description for the Malaria model

Variable and Parameters	Description
$S_h(t)$	Number of susceptible humans at time t.
$E_h(t)$	Number of exposed humans at time t.
$I_h(t)$	Number of infected humans at time t.
$T_h(t)$	Number of treated humans at time t.
$R_h(t)$	Number of recovered humans at time t.
$S_v(t)$	Number of susceptible vector at time t.
$E_v(t)$	Number of exposed vector at time t.
$I_v(t)$	Number of infected vector at time t
$N_h(t)$	Total number of human population at time t.
$N_v(t)$	Total number of vector population at time t.
π_h	Recruitment rate of humans.
ψ	Rate of loss of immunity.
α_h	Force of infection of humans from susceptible state to exposed state.
μ_h	Natural death rate for humans.
κ_h	Rate of progression of humans from the exposed state to the infectious state.
τ	Treatment of humans from the infectious state to the recovered state.
r	Recovery rate of infected humans.
ε	Progression rate from treated to recovered class
π_v	Recruitment rate of vector.
α_v	Force of infection of vector from susceptible state to exposed state.
μ_v	Natural death rate for vector.
δ	Disease-induced death rate for humans.
κ_v	Rate of progression of vector from the exposed state to the infectious state.
β_{vh}	Probability of transmission of infection from an infectious vector to a susceptible human provided there is a bite.
β_{hv}	The probability of transmission of infection from an infectious human to a susceptible vector provided there is a bite.
ϕ	Biting rate of vector.

The total population sizes are $N_h = \mathrm{S_h} + E_h + I_h + T_h + R_h$ and $N_v = S_v + E_v + I_v$ with their differential equations

$$\left.\begin{aligned} \frac{dN_h}{dt} &= \frac{dS_h}{dt} + \frac{dE_h}{dt} + \frac{dI_h}{dt} + \frac{dT_h}{dt} + \frac{dR_h}{dt} \\ &= \pi_h - \mu_h N_h - \delta I_h \end{aligned}\right. \quad \textit{and} \quad \left.\begin{aligned} \frac{dN_v}{dt} &= \frac{dS_v}{dt} + \frac{dE_v}{dt} + \frac{dI_v}{dt} \\ &= \pi_v - \mu_v N_v \end{aligned}\right\} \tag{3.2}$$

3 INVARIANT REGION

The invariant region can be obtained by the following theorem.

Theorem 1: The solutions of the model (2.9) are feasible for all $t > 0$ if they enter the invariant region $\Omega = \Omega_h \times \Omega_v$.

Proof: Let $\Omega = (S_h, E_h, I_h, T_h, R_h, S_v, E_v, I_v,) \in R_+^8$ be any solution of the system (3.1) with non-negative initial conditions. In absence of the malaria ,i.e. $I_h = 0$, equation (3.2)

Hence all feasible solution set of the human population of the malaria model enters the region

$$\Omega_h = \left\{ (S_h, E_h, I_h, T_h, R_h) \in R_+^5 : S_h \geq 0, E_h \geq 0 \;\; I_h \geq 0, T_h \geq 0, R_h \geq 0, N_h \leq \frac{\pi_h}{\mu_h} \right\}.$$

Similarly, the feasible solution set of the vector population enter the region

$$\Omega_v = \left\{ (S_v, E_v, I_v,) \in R_+^3 : S_v \geq 0, E_v \geq 0, I_v \geq 0, N_v \leq \frac{\pi_v}{\mu_v} \right\}.$$

Therefore, the region Ω is positively invariant i.e. solution remains positive for all temporal values.

Thus, the model (3.1) is biologically meaningful and mathematical well-posed or well present in the domain Ω.

3.1 BASIC REPRODUCTION NUMBER R_0

We use the next generation operator approach as described by [10] to define the basic reproduction number, R_0, as the number of secondary infections that one infectious individual would create over the duration of the infectious period, provided that everyone else is susceptible. Finally the basic reproduction number R_0 is given by

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{\beta_{vh}\phi\pi_h\mu_v}{\pi_v\mu_h} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_{hv}\phi\pi_v\mu_h}{\pi_h\mu_v} & \frac{\beta_{hv}\phi\eta\pi_v\mu_h}{\pi_h\mu_v} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \kappa_h + \mu_h & 0 & 0 & 0 \\ -\kappa_h & r + \mu_h + \delta + \tau & 0 & 0 \\ 0 & 0 & \kappa_v + \mu_v & 0 \\ 0 & 0 & -\kappa_v & \mu_v \end{pmatrix}$$

Therefore,

$$R_0 = \sqrt{\frac{\beta_{vh}\phi\pi_h\kappa_v}{\pi_v\mu_h(\kappa_v + \mu_v)}\left(\frac{\beta_{hv}\phi\pi_v\mu_h}{\pi_h\mu_v(\kappa_h + \mu_h)} + \frac{\beta_{hv}\phi\eta\pi_v\mu_h\kappa_h}{\pi_h\mu_v(\kappa_h + \mu_h)(r + \mu_h + \delta + \tau)}\right)} \tag{3.3}$$

3.2 LOCAL STABILITY OF THE DISEASE FREE EQUILIBRIUM

The local stability of the disease-free equilibrium can be analyzed using the Jacobian matrix of the malaria model at the disease free equilibrium point. Using [27], the following theorem holds.

Theorem 2: The disease free equilibrium point for the model (3.1) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: The Jacobian matrix (J) of the malaria model (3.1) with $S_h = N_h - (E_h + I_h + T_h + R_h)$ and $S_v = N_v - (E_v + I_v)$ at the disease-free equilibrium point is given by

$$J(E_0) = \begin{bmatrix} -(\kappa_h + \mu_h) & 0 & 0 & 0 & 0 & \frac{\beta_{vh}\phi\pi_v\mu_h}{\pi_h\mu_v} \\ \kappa_h & -(r + \mu_h + \delta + \tau) & 0 & 0 & 0 & 0 \\ 0 & \tau & -(\varepsilon + \mu_h) & 0 & 0 & 0 \\ 0 & r & \varepsilon & -(\psi + \mu_h) & 0 & 0 \\ \frac{\beta_{hv}\phi\pi_v\mu_h}{\pi_h\mu_v} & \frac{\beta_{hv}\phi\eta\pi_v\mu_h}{\pi_h\mu_v} & 0 & 0 & -(\kappa_v + \mu_v) & 0 \\ 0 & r & 0 & 0 & \kappa_v & -\mu_v \end{bmatrix} \tag{3.4}$$

The eigenvalues of the Jacobian matrix are the solutions of the characteristic equation $|J-\lambda I|=0$.

This implies

$$(\lambda+A_1)(\lambda+A_2)(\lambda+A_3)(\lambda+A_4)+(\lambda+A_1)\frac{r\kappa_h\beta_{vh}\phi\pi_v\mu_h}{\pi_h A_3}-\frac{\kappa_v\kappa_h\beta_{vh}\beta_{hv}\phi^2\eta\pi_v^2\mu_h^2}{\pi_h^2A_3^2}+(\lambda+A_4)\frac{\kappa_v\beta_{hv}\phi\pi_v\mu_h}{\pi_h A_3}=0$$

Where $A_1=\kappa_v+\mu_v$, $A_2=\kappa_h+\mu_h$, $A_3=\mu_v$, $A_4=r+\mu_h+\delta+\tau$

which is equivalent to the polynomial

$$B_0\lambda^4+B_1\lambda^3+B_2\lambda^2+B_3\lambda+B_4=0 \tag{3.5}$$

Where

$$\left.\begin{aligned}
B_1&=A_1+A_2+A_3+A_4\\
B_2&=A_1A_2+A_1A_3+A_1A_4+A_2A_3+A_2A_4+A_3A_4\\
B_3&=A_2A_3A_4+A_1A_3A_4+A_1A_2A_4+A_1A_2A_3+\frac{r\kappa_h\beta_{vh}\phi\pi_v\mu_h}{\pi_h A_3}+\frac{A_4\kappa_v\beta_{hv}\phi\pi_v\mu_h}{\pi_h A_3}\\
B_4&=A_1A_2A_3A_4+\frac{A_1r\kappa_h\beta_{vh}\phi\pi_v\mu_h}{\pi_h A_3}-\frac{\kappa_v\kappa_h\beta_{vh}\beta_{hv}\phi^2\eta\pi_v^2\mu_h^2}{\pi_h^2A_3^2}+\frac{A_4\kappa_v\beta_{hv}\phi\pi_v\mu_h}{\pi_h A_3}
\end{aligned}\right\} \tag{3.6}$$

Since solving the above characteristic polynomial for eigenvalues is tedious we will use the Routh-Hurwitz criterion to determine whether all roots have negative real parts and establish the stability of the system without solving the characteristic equation itself. We use the following lemma.

Lemma 1 (**Routh-Hurwitz criterion**): The roots of the characteristic equation have negative real parts if and only if all the principal diagonal minors of the Hurwitz matrix are positive provided that $B_0>0$. For our case of a fourth order system, the stability criterion is defined by the inequalities

$B_0>0$, $B_1>0$, $B_2>0$, $B_3>0$, $B_4>0$

and $\det(H_1)=B_1>0$, $\det(H_2)=\begin{pmatrix}B_1&1\\0&B_2\end{pmatrix}=B_1B_2>0$, $\det(H_3)=\begin{pmatrix}B_1&1&0\\B_3&B_2&B_1\\0&0&B_3\end{pmatrix}=B_1B_2B_3-B_3^2>0\Rightarrow B_1B_2-B_3>0$

and $\det(H_4)=\begin{pmatrix}B_1&1&0&0\\B_3&B_2&B_1&1\\0&B_4&B_3&B_2\\0&0&0&B_4\end{pmatrix}=B_3(B_2B_1-B_3)-B_4B_1^2>0$.

Since all the determinants of the Hurwitz matrices are positive, then it means all the eigenvalues of the Jacobian (3.4) have negative real part and $R_0<1$. Therefore, disease-free equilibrium point is stable.

3.3 THE ENDEMIC EQUILIBRIUM POINT

Endemic equilibrium points are steady state solutions where the disease persists in the population (all state variables are positive). That is, $E^*=\left(S_h^*,E_h^*,I_h^*,T_h^*,R_h^*,S_v^*,E_v^*,I_v^*,\right)>0$ this is obtained by setting the right hand side of (2.9) to zero and solve, we have

$$\left.\begin{aligned}
&S_h^*=\frac{\kappa_h\phi_1\varepsilon\psi\tau-\phi_1K_1K_2K_3K_4+\pi_hK_1K_2K_3K_4+\psi r\phi_1K_3\kappa_h}{\mu_hK_1K_2K_3K_4},\quad E_h^*=\frac{\phi_1}{K_1},\qquad I_h^*=\frac{\kappa_h\phi_1}{K_1K_2},\\
&T_h^*=\frac{\tau\kappa_h\phi_1}{K_1K_2K_3},\quad R_h^*=\frac{\phi1\kappa_h(\tau\varepsilon+rK_3)}{K_1K_2K_3K_4},\qquad S_v^*=\frac{-\phi_2-\pi_v}{\mu_v},E_v^*=\frac{\phi_2}{K_5},I_v^*=\frac{\kappa_v\phi_2}{\mu_vK_5}
\end{aligned}\right\} \tag{3.7}$$

Where $K_1 = \kappa_h + \mu_h, K_2 = r + (\mu_h + \delta) + \tau, K_3 = \varepsilon + \mu_h, K_4 = \psi + \mu_h, K_5 = \kappa_v + \mu_v$

$\phi_1 = \frac{\beta_{vh}\phi I_v S_h}{N_v}$, $\phi_2 = \frac{\beta_{hv}\phi(E_h + \eta I_h)S_v}{N_h}$.

3.4 NUMERICAL SIMULATION

A numerical simulation of the model was performed for better understanding of dynamic spreads of the malaria in human and vector populations. The simulation is conducted using a fourth order Runge-kutta scheme in Maple 17 software.

The parameter values defined in Table 3 were used with the initial conditions

$S_h(0) = 13{,}000$, $E_h(0) = 8{,}000$, $I_h(0) = 5{,}000$, $T_h(0) = 4{,}000$, $R_h(0) = 3{,}000$, $S_v(0) = 9{,}000$, $E_v(0) = 7{,}000$, $I_v(0) = 5{,}000$

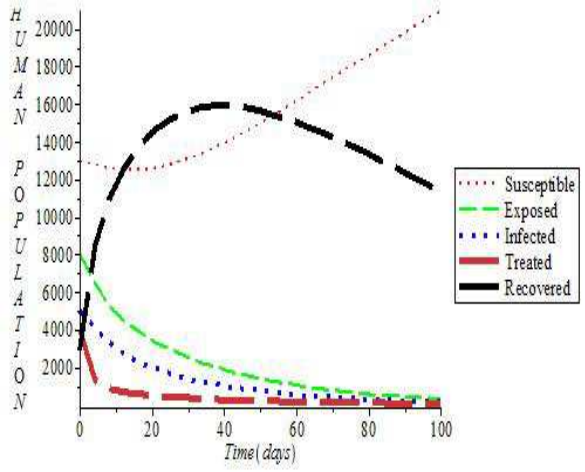

Fig. 1. The graph of dynamic spreads of malaria in human compartments

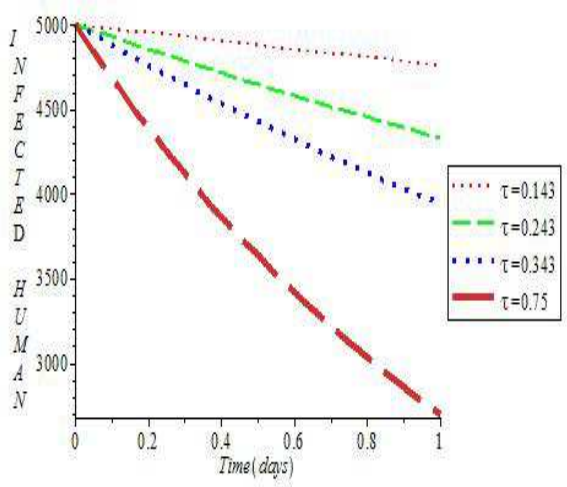

Fig. 2. The graph of dynamic infected human at different treatment rate

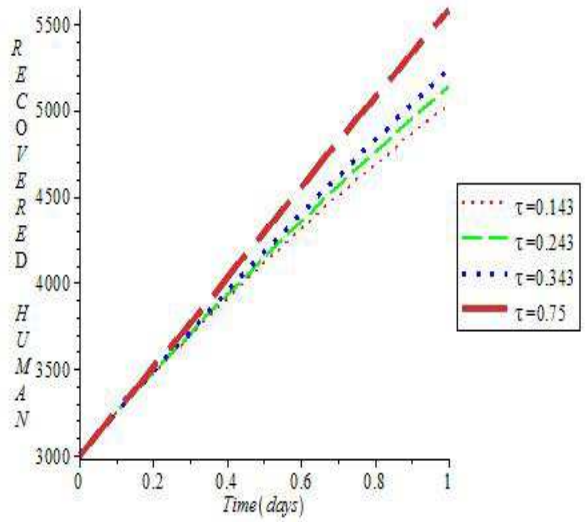

Fig. 3. The graph of recoverd human at different treatment rate

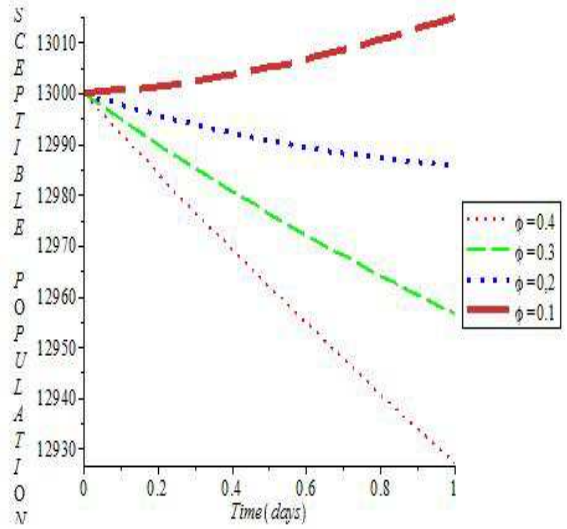

Fig. 4. The graph of susceptible human at different values of biting rate

3.5 DISCUSSION OF RESULT AND CONCLUSION

Eight (8) new compartmental models were formulated to gain more insight into the dynamical spread of malaria. It showed the existence and uniqueness of a domain where the model is epidemiologically and mathematically well-presented. The model was analyzed for the disease free equilibrium and endemic equilibrium. Basic reproduction number 'R_0' which is the baseline to determine whether the disease will die out or spread was calculated using next generation matrix method, the result shows that, disease dies out whenever the threshold $R_0 < 1$ but spreads when it exceeds unity i.e. $R_0 > 1$. Also, numerical simulations illustrate that Figure 1: shows the distribution of human population with times in all classes. It is found that initially the proportion of susceptible population decreases slightly in early childhood and increases gently to finally reach its equilibrium this is due to treatment, as a result of that infection is minimized in childhood. In the initial stage of treatment population, we observed that the treatment population was high this is attributed to the progression rate of treatment of individual from malaria. After some times, we again see that the treatment population decreases steadily and then remained constant for some times, this is because individuals who are accessing treatment are now leaving the treated class to recovered class.

Recovered population increases due to the fact that those who are infected leaving the treated class after receiving the treatment and remain constant for some times but later decline because of loss immunity.

Figure 2: illustrates the change in infected human at different treatment rate. Infected population initially was high but as the treatment increases some children recovers and others die.

Figure 3: illustrates the change in recovered human at different treatment rate. Recovered population increased as the infected class is reduced due to increase in treatment.

Figure 4: illustrates the change in susceptible population at different values of biting rate. Susceptible population was reduced due to the biting rate of infectious vector as the biting rate is reducing susceptible becoming high.

Conclusively, the most effective strategies for controlling malaria are to reduce the vector biting rate and increased the human treatment.

Table 3: Shows the estimated parameters and their sources for the model (3.1). The rates are given per day.

Symbol	Value	Source
π_h	0.000051	[5]
ψ	0.011	Assumed
μ_h	0.000043	[26]
κ_h	0.071	[30]
τ	0.143	[23]
r	0.02	[1]
ε	0.6	Assumed
π_v	0.071	[20]
μ_v	0.04	Assumed
δ	0.0000027	[28]
κ_v	0.091	[8]
β_{vh}	0.066	Assumed
β_{hv}	0.42	Assumed
ϕ	0.4	[8]
η	0.02	Assumed

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