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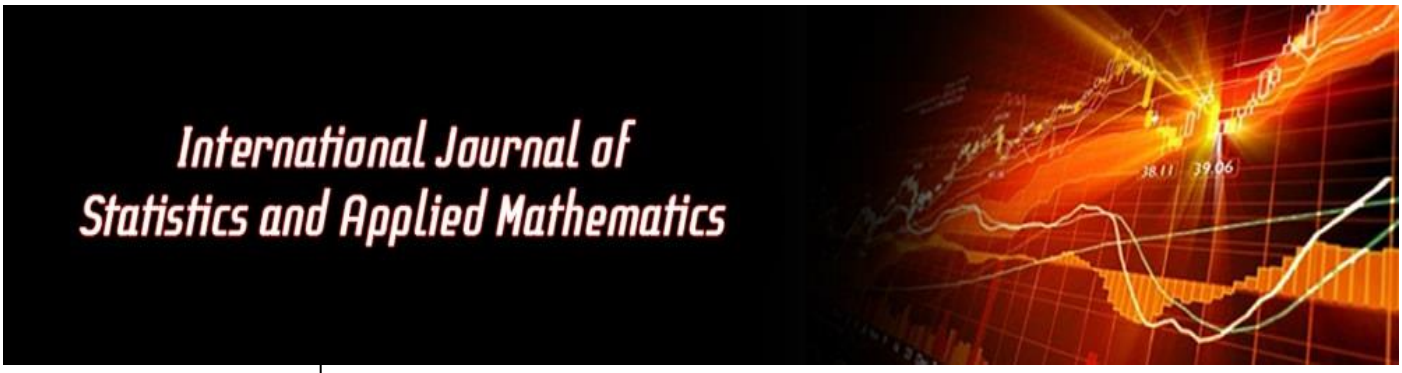

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Stability analysis of disease free equilibrium (DFE) state of a mathematical model of malaria disease in the presence of drug therapy and treatment

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Abstract
In this paper, we propose a mathematical model of malaria disease in the presence of drug therapy and treatment. We obtained the Disease Free Equilibrium (DFE) points and compute the effective reproduction number (R_{eff}). The local and global stability of the DFE was analyzed using the approaches of Jacobian Matrix t analysis and Lyapunov function respectively. The local and global stability is asymptotically stable if $R_{eff} < 1$ and $R_{eff} \leq 1,$ respectively. The effective reproduction number, drug therapy and treatment were numerically simulated and the results are presented in graphical form.

Keywords: Stability analysis, DFE, mathematical model, malaria disease, drug therapy, treatment

1. Introduction
Malaria disease is caused by *Plasmodium* parasites. The parasites are spread to people through the bites of an infected female *Anopheles* mosquito known as malaria vector. In [1] 219 million cases of malaria were estimated in 89 countries by World Health Organization (WHO). The estimated number of malaria deaths stood at 435,000 in 2017 as given by [1] that African region carries a disproportionately high share of the global malaria burden. Their statistics showed that in 2017, the region was placed on 92 percent of malaria cases and 93 percent of malaria deaths. In 2010, WHO estimated that 216 million cases of malaria occurred worldwide and 81 percent was recorded percentage of African region. WHO facts reviewed that in 2010, there were 655,000 malaria deaths, 91 percent in the African region, and 86 percent were children under 5 years of age. WHO [2] reported that malaria affects 3.3 billion people and half of the world's population in 106 countries, malaria is the third leading cause of death most especially for children under five years worldwide, after pneumonia and diarrheal disease. Thirty countries in sub-Saharan Africa account for 90 percent of global malaria deaths. Nigeria, Democratic Republic of Congo (DRC), Ethiopia, and Uganda account for nearly 50 percent of the global malaria deaths. Malaria disease is the second leading cause of death from infectious diseases in Africa, after HIV/AIDS. Almost 1 out of 5 deaths of children under 5 in Africa are due to malaria.
In this work, we propose a deterministic mathematical model of malaria dynamics which is a system of Fractional Differential Equations (FDEs) to investigate the behavior of drug therapy and treatment rate on effective reproduction number. We consider the probability of receiving treatment p at the time of acquiring infection rather than the time of infection, as an alternative way of capturing the proportion of infections that are treated. The total time to move from being infectious to becoming susceptible again is $(q+\tau)$ and hence the populations who receive drug therapy q do so at a rate of $p \times 1/(q+\tau)$. The populations that are infectious but remain untreated recovered naturally at $((1-p)/\delta)$. However, as pointed out in [3, 4], an infection with malaria is a lifelong disease since the infected

individual harbored the virus in the blood for at least more than a year. With malaria, infected individuals return to the susceptible class on recovery because the disease confers no immunity against re-infection. Some fractions of susceptible proportion, latent proportion and symptomatic proportion are placed on a regular time to seek drug therapy at an equal rate of σ_3. This is simply because 97 percent of Nigerians are infected with malaria virus from mosquitoes bite. And we assume that all infected individuals who recovered naturally at the rate $((1-p)/\delta)$, symptomatic individuals that do not access drug therapy and treatment at a rate $1/\alpha_0$ and those who only take drug therapy may enter latent compartment and can be considered as latently infected individuals. We allow the reproduction rate of malaria virus from the mosquitoes bite to enter the model. Therefore, susceptible individuals are allowed to be either under drug therapy or latent with certain probabilities.

2. Material and Methods

2.1 Formulation of the Model Equations

We formulate a mathematical model for malaria where the population is partitioned into six compartments of the Susceptible $S(t)$; Latent $L(t)$; Symptomatic $B(t)$; Infected $I(t)$; Drug therapy $Q(t)$; while the sixth class is the Treatment $T(t)$. Patients may seek drug therapy when symptoms have manifested as well as at the infectious stage, and a person may be re-infected once susceptible again. The natural recovery period is assumed to be longer than the drug recovery period and the time to infectiousness. Probability of receiving treatment *p* is applied at the time of acquiring infection rather than during the infection. The classes susceptible, latent and symptomatic seek drug therapy at a regular rate σ_3. After the drug therapy, individual may move to either susceptible, latent or treatment class depending on whether the malaria viruses are cleared, hidden or persist. Time to seek treatment after drug therapy is not equal time to seek treatment during infection; becoming susceptible again is the combined effects of treatment, drug therapy and recovery rate per infected individual. Reproduction rate of malaria virus and death removal rate are not equal. Disease induce death rate is applicable to only infected class. Those who recovered naturally δ without drug and treatment moved into latent class. We assumed the malaria virus is not cleared in their body and the influx of malaria virus reproduction at a rate β, natural death is applicable to all the compartments at a rate μ_0, disease induce death is applicable to only infectious class at a rate μ_1 and latent rate α_0 relative to infection by symptomatic class. The population N is compartmentalized into the proportions of susceptible, latent, symptomatic, infected, drug therapy, and treatment class.

2.2 Model Equations

$$\frac{dS}{dt} = \frac{1}{\beta} + \frac{1}{q}Q + \frac{1}{(\alpha+\gamma)}T - \left(\frac{1-\varepsilon}{\sigma_0} + \frac{\varepsilon}{\sigma_3} + \frac{1}{\mu_0}\right)S \tag{1}$$

$$\frac{dL}{dt} = \frac{1-\varepsilon}{\sigma_0}S + \left(\frac{1}{\delta(1-p)}I + \frac{1}{\alpha_0}B + \frac{1}{\sigma_4}\right)Q - \left(\frac{\theta}{\sigma_3} + \frac{1-\theta}{\sigma_1} + \frac{1}{\mu_0}\right)L \tag{2}$$

$$\frac{dB}{dt} = \frac{1-\theta}{\sigma_1}L - \left(\frac{\nu}{\sigma_3} + \frac{1-\nu}{\sigma_2} + \frac{1}{\mu_0}\right)B \tag{3}$$

$$\frac{dI}{dt} = \frac{1-\nu}{\sigma_2}B - \left(\frac{1}{(\tau+p)} + \frac{1}{(\mu_0+\mu_1)}\right)I \tag{4}$$

$$\frac{dQ}{dt} = \frac{1}{\sigma_3}(\varepsilon S + \theta L + \nu B) - \left(\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}\right)Q \tag{5}$$

$$\frac{dT}{dt} = \frac{1}{(\tau+p)}I + \frac{1}{\tau_0}Q - \left(\frac{1}{(\alpha+\gamma)} + \frac{1}{\mu_0}\right)T \tag{6}$$

$$S(0) \geq 0, L(0) \geq 0, B(0) \geq 0, I(0) \geq 0, Q(0) \geq 0, T(0) \geq 0.$$

$$S(t) + L(t) + B(t) + I(t) + Q(t) + T(t) = 1 \tag{7}$$

The model is defined in the subset $D \times [0, \infty)$ of $\Re_+^6$, where

$$D = \left\{(S, L, B, I, Q, T) \in \Re_+^6 : 0 \leq S, L, B, I, Q, T \leq 1, S + L + B + I + Q + T \leq 1\right\}$$

Table 1: Notation and definition of variables and parameter are represented as follows

Symbols	Description
$S(t)$	Susceptible individuals at time t
$L(t)$	Latent period at time t
$B(t)$	Symptomatic individuals at time t
$I(t)$	Latent period at time t
$Q(t)$	Drug therapy period at time t
$T(t)$	Treatment period at time t
σ_0	Period of susceptible
σ_1	Period of latent
σ_2	Time of infectiousness
σ_3	Time to seek drug therapy
σ_4	Latent period after drug therapy
τ_0	Time to seek treatment after drug therapy
τ	Time to seek treatment
β	Reproduction rate of malaria virus
μ_0	Natural death rate
μ_1	Death rate of Infected
α	Treatment rate
α_0	Latent rate relative to infection by symptomatic class
γ	Rate of recovery
ε	Susceptible proportions that seek drug therapy at σ_3
θ	Latent proportions that seek drug therapy at σ_3
ν	Symptomatic proportions that seek drug therapy at σ_3
q	Drug recovery period
δ	Natural recovery period
p	Probability of treatment
N	Population size
$\delta(1-p)$	Rate of moving from infected to latent when there is no drug therapy and treatment

3. Existence of Equilibrium points of the model

In order to investigate the existence of equilibrium points for equation (1) to (6), we shall express (1) to (6) in form of (8) to (13) for ease of analysis as follows

$$S'(t) = f_0 + f_1 Q + f_2 T - (f_3 + f_4 + f_5)S \tag{8}$$

$$L'(t) = f_3 S + (f_6 I + f_7 B + f_8)Q - (f_9 + f_{10} + f_5)L \tag{9}$$

$$B'(t) = f_{10} L - (f_{11} + f_{12} + f_5)B \tag{10}$$

$$I'(t) = f_{12} B - (f_{13} + f_{14})I \tag{11}$$

$$Q'(t) = f_{15}(\varepsilon S + \theta L + \nu B) - (f_1 + f_{16} + f_8 + f_5)Q \tag{12}$$

$$T'(t) = f_{13} I + f_{16} Q - (f_2 + f_5)T \tag{13}$$

Where,

$$\left.\begin{aligned} &f_0=\frac{1}{\beta}, f_1=\frac{1}{q}, f_2=\frac{1}{\alpha+\gamma}, f_3=\frac{1-\varepsilon}{\sigma_0}, f_4=\frac{\varepsilon}{\sigma_3}, f_5=\frac{1}{\mu_0}, \\ &f_6=\frac{1}{\delta(1-p)}, f_7=\frac{1}{\alpha_0}, f_8=\frac{1}{\sigma_4}, f_9=\frac{\theta}{\sigma_3}, f_{10}=\frac{1-\theta}{\sigma_1}, f_{11}=\frac{\nu}{\sigma_3}, \\ &f_{12}=\frac{1-\nu}{\sigma_2}, f_{13}=\frac{1}{\tau+p}, f_{14}=\frac{1}{\mu_0+\mu_1}, f_{15}=\frac{1}{\sigma_3}, f_{16}=\frac{1}{\tau_0} \end{aligned}\right\} \quad (14)$$

According to [5], equilibria are the points where the variables do not change with time. Thus,

$$\frac{dS}{dt}=\frac{dL}{dt}=\frac{dB}{dt}=\frac{dI}{dt}=\frac{dQ}{dt}=\frac{dT}{dt}=0 \quad (15)$$

Let,

$$(S,L,B,I,Q,T)=(S^*,L^*,B^*,I^*,Q^*,T^*), \quad (16)$$

be the arbitrary equilibrium point. Therefore, the system (8) to (13) becomes

$$f_0+f_1Q^*+f_2T^*-(f_3+f_4+f_5)S^*=0 \quad (17)$$

$$f_3S^*+(f_6I^*+f_7B^*+f_8)Q^*-(f_9+f_{10}+f_5)L^*=0 \quad (18)$$

$$f_{10}L^*-(f_{11}+f_{12}+f_5)B^*=0 \quad (19)$$

$$f_{12}B^*-(f_{13}+f_{14})I^*=0 \quad (20)$$

$$f_{15}(\varepsilon S^*+\theta L^*+\nu B^*)-(f_1+f_{16}+f_8+f_5)Q^*=0 \quad (21)$$

$$f_{13}I^*+f_{16}Q^*-(f_2+f_5)T^*=0 \quad (22)$$

From equations (17), (19), (20) and (22), we have:

$$L^*=\frac{(f_{11}+f_{12}+f_5)B^*}{f_{10}} \quad (23)$$

$$I^*=\frac{f_{12}B^*}{(f_{13}+f_{14})} \quad (24)$$

From (22) and (24), we obtain:

$$Q^*=\frac{(f_2+f_5)T^*}{f_{16}}-\frac{f_{12}f_{13}B^*}{f_{16}(f_{13}+f_{14})} \quad (25)$$

From (17) and (25), we obtain:

$$S^*=\frac{f_0}{(f_3+f_4+f_5)}+\left(\frac{f_2}{(f_3+f_4+f_5)}+\frac{f_1(f_2+f_5)}{f_{16}(f_7+f_6+f_5)}\right)T^*-\frac{f_1f_{12}f_{13}B^*}{f_{16}(f_{13}+f_{14})(f_3+f_4+f_5)} \quad (26)$$

Substituting (23), (24), (25) and (26) into (18) and simplifying, we have:

$$\left(\frac{f_0 f_3}{(f_3+f_4+f_5)}\right)+\left[\left(\frac{f_2 f_3}{(f_3+f_4+f_5)}+\frac{f_1 f_3(f_2+f_5)}{f_{16}(f_3+f_4+f_5)}\right)+\left(\frac{f_6 f_{12}B^*}{(f_{13}+f_{14})}+f_7B^*+f_8\right)\left(\frac{(f_2+f_5)}{f_{16}}\right)\right]T^*$$

$$-\left[\left(\frac{f_1 f_3 f_{12} f_{13}}{f_{16}(f_{13}+f_{14})(f_3+f_4+f_5)}\right)+\left(\frac{f_6 f_{12}B^*}{(f_{13}+f_{14})}+f_7B^*+f_8\right)\left(\frac{f_{12} f_{13}}{f_{16}(f_{13}+f_{14})}\right)\right.$$
$$\left.+\left(\frac{(f_9+f_{10}+f_5)(f_{11}+f_{12}+f_5)}{f_{10}}\right)\right]B^*=0 \quad (27)$$

Substituting (23), (25) and (26) into (21) and simplifying, we have:

$$\left(\frac{\varepsilon f_{15} f_0}{(f_3+f_4+f_5)}\right)+\left[\left(\frac{\varepsilon f_2 f_{15}}{(f_3+f_4+f_5)}\right)+\left(\frac{\varepsilon f_1 f_{15}(f_2+f_5)}{f_{16}(f_3+f_4+f_5)}\right)-\left(\frac{(f_1+f_{16}+f_8+f_5)(f_2+f_5)}{f_{16}}\right)\right]T^*$$

$$-\left[\left(\frac{\varepsilon f_1 f_{15} f_{12} f_{13}}{f_{16}(f_{13}+f_{14})(f_3+f_4+f_5)}\right)-\left(\frac{\theta f_{15}(f_{11}+f_{12}+f_5)-f_{10} f_{15}\nu}{f_{10}}\right)-\left(\frac{f_{12} f_{13}(f_1+f_{16}+f_8+f_5)}{f_{16}(f_{13}+f_{14})}\right)\right]B^*=0 \quad (28)$$

In order to analyze the equilibria of the model, the expression in (27) and (28) are cumbersome therefore; as stated in [6], we examine the existence of equilibria in the neighbourhood of linear system of simultaneous equations given in (29) to (30) as:

$$a(t)T^*+b(t)B^*=c(t) \quad (29)$$

$$e(t)T^*+g(t)B^*=h(t) \quad (30)$$

Where,

$$a(t)=\left[\left(\frac{f_2 f_3}{(f_3+f_4+f_5)}+\frac{f_1 f_3(f_2+f_5)}{f_{16}(f_3+f_4+f_5)}\right)+\left(\frac{f_6 f_{12}B^*}{(f_{13}+f_{14})}+f_7B^*+f_8\right)\left(\frac{(f_2+f_5)}{f_{16}}\right)\right] \quad (31)$$

$$b(t)=-\left[\left(\frac{f_1 f_3 f_{12} f_{13}}{f_{16}(f_{13}+f_{14})(f_3+f_4+f_5)}\right)+\left(\frac{f_6 f_{12}B^*}{(f_{13}+f_{14})}+f_7B^*+f_8\right)\left(\frac{f_{12} f_{13}}{f_{16}(f_{13}+f_{14})}\right)\right.$$
$$\left.+\left(\frac{(f_9+f_{10}+f_5)(f_{11}+f_{12}+f_5)}{f_{10}}\right)\right] \quad (32)$$

$$c(t)=-\left(\frac{f_0 f_3}{(f_3+f_4+f_5)}\right) \quad (33)$$

$$e(t)=\left[\left(\frac{\varepsilon f_2 f_{15}}{(f_3+f_4+f_5)}\right)+\left(\frac{\varepsilon f_1 f_{15}(f_2+f_5)}{f_{16}(f_3+f_4+f_5)}\right)-\left(\frac{(f_1+f_{16}+f_8+f_5)(f_2+f_5)}{f_{16}}\right)\right] \quad (34)$$

$$g(t)=-\left[\left(\frac{\varepsilon f_1 f_{15} f_{12} f_{13}}{f_{16}(f_{13}+f_{14})(f_3+f_4+f_5)}\right)-\left(\frac{\theta f_{15}(f_{11}+f_{12}+f_5)-f_{10} f_{15}\nu}{f_{10}}\right)\right.$$
$$\left.-\left(\frac{f_{12} f_{13}(f_1+f_{16}+f_8+f_5)}{f_{16}(f_{13}+f_{14})}\right)\right] \quad (35)$$

$$h(t) = -\left(\frac{\varepsilon f_{15} f_0}{(f_3 + f_4 + f_5)}\right) \tag{36}$$

In order to make our argument valid we deduce that equilibria solutions exist and are stable approximately [7], i.e.

$$n(t) \approx c(t) \approx h(t) \tag{37}$$

$$k(t) \approx a(t) \approx e(t) \tag{38}$$

Substituting (37) to (38) into (29) to (30) and simplifying, we obtain a condition for which (29) and (30) are in the form:

$$B^*\big(b(t) - g(t)\big) = 0 \tag{39}$$

and so this implies that either,

$$B^* = 0 \tag{40}$$

Or

$$\big(b(t) - g(t)\big) = 0 \tag{41}$$

Therefore, as in [8] from equation (39), we have existence of two different equilibria; one satisfying equation (40) where all the infected compartments are zero, while the other satisfying (41). Thus, substituting (40) into (19) and (20), we have:

$$L^* = B^* = I^* = 0 \tag{42}$$

3.1 Disease Free Equilibrium (DFE) points

Let,

$$E^0 = (S, L, B, I, Q, T) = \{S^0, L^0, B^0, I^0, Q^0, T^0\} \tag{43}$$

Substituting (42) into (17) to (22) give:

$$f_0 + f_1 Q^* + f_2 T^* - (f_3 + f_4 + f_5) S^* = 0 \tag{44}$$

$$f_3 S^* + f_8 Q^* = 0 \tag{45}$$

$$\varepsilon f_{15} S^* - (f_1 + f_{16} + f_8 + f_5) Q^* = 0 \tag{46}$$

$$f_{16} Q^* - (f_2 + f_5) T^* = 0 \tag{47}$$

Solving (44) to (47), we have that a DFE exist at the point

$$(S^0, L^0, B^0, I^0, Q^0, T^0) = \{W_0, 0, 0, 0, W_1, W_2\} \tag{48}$$

Where,

$$W_0 = S^0 = \frac{\left(\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}\right)\sigma_3}{\beta\left(\frac{\left(\frac{1}{1-\varepsilon} + \frac{\varepsilon}{\sigma_3} + \frac{1}{\mu_0}\right)\left(\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}\right)\sigma_3}{\varepsilon} - \frac{1}{(\alpha+\gamma)\tau_0\left(\frac{1}{\alpha+\gamma} + \frac{1}{\mu_0}\right)} - \frac{1}{q}\right)\varepsilon} \tag{49}$$

$$W_1 = Q^0 = \frac{1}{\beta\left(\frac{\left(\frac{1}{1-\varepsilon}+\frac{\varepsilon}{\sigma_3}+\frac{1}{\mu_0}\right)\left(\frac{1}{q}+\frac{1}{\tau_0}+\frac{1}{\sigma_4}+\frac{1}{\mu_0}\right)\sigma_3}{\varepsilon} - \frac{1}{(\alpha+\gamma)\tau_0\left(\frac{1}{\alpha+\gamma}+\frac{1}{\mu_0}\right)} - \frac{1}{q}\right)} \tag{50}$$

$$W_2 = T^0 = \frac{\left(\frac{1}{\tau_0}\right)\left(\frac{1}{\beta\left(\frac{\left(\frac{1}{1-\varepsilon}+\frac{\varepsilon}{\sigma_3}+\frac{1}{\mu_0}\right)\left(\frac{1}{q}+\frac{1}{\tau_0}+\frac{1}{\sigma_4}+\frac{1}{\mu_0}\right)\sigma_3}{\varepsilon} - \frac{1}{(\alpha+\gamma)\tau_0\left(\frac{1}{\alpha+\gamma}+\frac{1}{\mu_0}\right)} - \frac{1}{q}\right)}\right)}{\frac{1}{\alpha+\gamma}+\frac{1}{\mu_0}} \tag{51}$$

Equation (48) is the DFE points.

3.2 Effective Reproduction Number, R_{eff}

For SEIR models, the rate of appearance of new infections is given by the new infection terms in the latent compartment [9, 10, 11]. From the equations (1) to (7) of the model, we have the vector $F(x)$ of the rates of new infections in compartments $L(t)$, $B(t)$ and $I(t)$ given as:

$$F(x) = \begin{pmatrix} \frac{1-\varepsilon}{\sigma_0}S + \left(\frac{1}{\delta(1-p)}I + \frac{1}{\alpha_0}B + \frac{1}{\sigma_4}\right)Q \\ 0 \\ 0 \end{pmatrix} \tag{52}$$

Also, the remaining transfer terms in compartments L, B and I is given by equation (53).

$$V(x) = \begin{pmatrix} \left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)L \\ -\frac{1-\theta}{\sigma_1}L + \left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)B \\ -\frac{1-\nu}{\sigma_2}B + \left(\frac{1}{(\tau+p)}+\frac{1}{(\mu_0+\mu_1)}\right)I \end{pmatrix} \tag{53}$$

The matrix of partial derivatives of $F(x)$ at DFE State, $\bar{x} = E_0 = (S_0, 0, 0, 0, Q_0, T_0)$ is given by

$$F_x(E_0)=\begin{pmatrix} 0 & \frac{1}{\alpha_0}Q_0 & \frac{1}{\delta(1-p)}Q_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \tag{54}$$

$$Q_0=\frac{1}{\beta\left(\frac{\left(\frac{1}{1-\varepsilon}+\frac{\varepsilon}{\sigma_3}+\frac{1}{\mu_0}\right)\left(\frac{1}{q}+\frac{1}{\tau_0}+\frac{1}{\sigma_4}+\frac{1}{\mu_0}\right)\sigma_3}{\varepsilon}-\frac{1}{(\alpha+\gamma)\tau_0\left(\frac{1}{\alpha+\gamma}+\frac{1}{\mu_0}\right)}-\frac{1}{q}\right)} \tag{55}$$

And the matrix of partial derivatives of $V(x)$ at DFE State $\bar{x}=E_0=(S_0,0,0,0,Q_0,T_0)$ is

$$V_x(E_0)=\begin{pmatrix} \frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0} & 0 & 0 \\ -\frac{1-\theta}{\sigma_1} & \frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0} & 0 \\ 0 & -\frac{1-\nu}{\sigma_2} & \frac{1}{\tau+p}+\frac{1}{\mu_0+\mu_1} \end{pmatrix} \tag{56}$$

It follows that the basic reproduction number R_0 is given by equation (57).

$$R_{eff}=\rho\left(F_xV^{-1}\right) \tag{57}$$

$$R_{eff}=\frac{(1-\theta)Q_0}{\alpha_0\sigma_1\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)}+\frac{(1-\theta)(1-\nu)Q_0}{\delta(1-p)\sigma_1\sigma_2\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)\left(\frac{1}{\tau+p}+\frac{1}{\mu_0+\mu_1}\right)} \tag{58}$$

4. Result and Discussion

4.1 Local Stability of Disease Free Equilibrium (DFE), E_0

Theorem 4.1. The Disease-Free Equilibrium of the model system (1) to (6) is locally asymptotically stable if $R_{eff}<1$ and unstable if $R_{eff}>1$

Proof:

We shall first compute the Jacobian matrix for the DFEs using equations (1) to (6). The Jacobian matrix for the disease-free state J_{E_0} is given as

$$J_{E_0}=\begin{pmatrix} -\left(\frac{1-\varepsilon}{\sigma_0}+\frac{\varepsilon}{\sigma_3}+\frac{1}{\mu_0}\right) & 0 & 0 & 0 & \frac{1}{q} & \frac{1}{\alpha+\gamma} \\ \frac{1-\varepsilon}{\sigma_0} & -\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right) & \frac{Q_0}{\alpha_0} & \frac{Q_0}{\delta(1-p)} & \frac{1}{\sigma_4} & 0 \\ 0 & \frac{1-\theta}{\sigma_1} & -\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right) & 0 & 0 & 0 \\ 0 & 0 & \frac{1-\nu}{\sigma_2} & -\left(\frac{1}{\tau+p}+\frac{1}{\mu_0+\mu_1}\right) & 0 & 0 \\ \frac{\varepsilon}{\sigma_3} & \frac{\theta}{\sigma_3} & \frac{\nu}{\sigma_3} & 0 & -\left(\frac{1}{q}+\frac{1}{\tau_0}+\frac{1}{\sigma_4}+\frac{1}{\mu_0}\right) & 0 \\ 0 & 0 & 0 & \frac{1}{\tau+p} & \frac{1}{\tau_0} & -\left(\frac{1}{\alpha+\gamma}+\frac{1}{\mu_0}\right) \end{pmatrix} \tag{59}$$

For ease of analysis, we perform the following operations on equation (59) and obtain (60).

$$J_{E_0} = \begin{pmatrix} k_1 & 0 & 0 & 0 & k_2 & k_3 \\ k_4 & k_5 & k_6 & k_7 & k_8 & 0 \\ 0 & k_9 & k_{10} & 0 & 0 & 0 \\ 0 & 0 & k_{11} & k_{12} & 0 & 0 \\ k_{13} & k_{14} & k_{15} & 0 & k_{16} & 0 \\ 0 & 0 & 0 & k_{17} & k_{18} & k_{19} \end{pmatrix} \tag{60}$$

Where,

$$\left.\begin{aligned} &k_1 = A_{11} = -\left(\frac{1-\varepsilon}{\sigma_0} + \frac{\varepsilon}{\sigma_3} + \frac{1}{\mu_0}\right), k_2 = A_{15} = \frac{1}{q}, k_3 = A_{16} = \frac{1}{\alpha+\gamma}, k_4 = \frac{1-\varepsilon}{\sigma_0}, \\ &k_5 = A_{22} = -\left(\frac{1-\theta}{\sigma_3} + \frac{\theta}{\sigma_1} + \frac{1}{\mu_0}\right), k_6 = A_{23} = \frac{Q_0}{\alpha_0}, k_7 = A_{24} = \frac{Q_0}{\delta(1-p)}, k_8 = \frac{1}{\sigma_4}, \\ &k_9 = \frac{1-\theta}{\sigma_1}, k_{10} = -\left(\frac{1-\nu}{\sigma_2} + \frac{\nu}{\sigma_3} + \frac{1}{\mu_0}\right), k_{11} = \frac{1-\nu}{\sigma_2}, k_{12} = -\left(\frac{1}{\tau+p} + \frac{1}{\mu_0+\mu_1}\right), \\ &k_{13} = \frac{\varepsilon}{\sigma_3}, k_{14} = \frac{\theta}{\sigma_3}, k_{15} = \frac{\nu}{\sigma_3}, k_{16} = -\left(\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}\right), k_{17} = \frac{1}{\tau+p}, \\ &k_{18} = \frac{1}{\tau_0}, k_{18} = -\left(\frac{1}{\alpha+\gamma} + \frac{1}{\mu_0}\right) \end{aligned}\right\} \tag{61}$$

Using Gaussian elimination row operation on the equation (60), we obtain the following

$$M = \begin{pmatrix} A_{11}-\lambda & 0 & 0 & 0 & A_{15} & A_{16} \\ 0 & A_{22}-\lambda & A_{23} & A_{24} & A_{25} & A_{26} \\ 0 & 0 & A_{33}-\lambda & A_{34} & A_{35} & A_{36} \\ 0 & 0 & 0 & A_{44}-\lambda & A_{45} & A_{46} \\ 0 & 0 & 0 & 0 & A_{55}-\lambda & A_{56} \\ 0 & 0 & 0 & 0 & 0 & A_{66}-\lambda \end{pmatrix} \tag{62}$$

Where,

$$\left.\begin{aligned} &A_{25} = \frac{k_1k_8 - k_2k_4}{k_1}, A_{26} = -\frac{k_3k_4}{k_1}, A_{33} = \frac{k_5k_{10} - k_6k_9}{k_5}, A_{34} = -\frac{k_7k_9}{k_5}, \\ &A_{35} = -\frac{A_{25}k_9}{k_5}, A_{36} = -\frac{A_{26}k_9}{k_5}, A_{44} = \frac{A_{33}k_{12} - A_{34}k_{11}}{A_{33}}, A_{45} = -\frac{A_{35}k_{11}}{A_{33}}, \\ &A_{46} = -\frac{A_{36}k_{11}}{A_{33}}, A_{55} = \frac{A_{44}B_0 - A_{45}B_1}{A_{44}}, A_{56} = \frac{A_{44}B_5 - A_{46}B_1}{A_{44}}, \\ &A_{66} = \frac{A_{55}B_6 - A_{56}B_7}{A_{55}} \end{aligned}\right\} \tag{63}$$

To simplify the notations, we let

$$\left.\begin{aligned} &B_0 = \frac{A_{33}B_2 - A_{35}B_3}{A_{33}}, B_1 = \frac{A_{33}B_4 - A_{34}B_3}{A_{33}}, B_2 = \frac{B_8k_5 - A_{25}k_{14}}{k_5}, \\ &B_3 = \frac{k_5k_{15} - k_6k_{14}}{k_5}, B_4 = -\frac{k_7 - k_{14}}{k_5}, B_5 = \frac{A_{33}B_9 - A_{36}B_3}{A_{33}}, \\ &B_6 = \frac{A_{44}k_{19} - A_{46}k_{17}}{A_{44}}, B_7 = \frac{A_{44}k_{18} - A_{45}k_{17}}{A_{44}}, B_8 = \frac{k_1k_{16} - k_2k_{13}}{k_1}, \\ &B_9 = -\frac{B_{10}k_5 - A_{26}k_{14}}{k_5}, B_{10} = -\frac{k_3k_{13}}{k_1} \end{aligned}\right\} \tag{64}$$

Therefore, the corresponding characteristic equation to M as defined by equation (62) yield:

$$(A_{11}-\lambda)(A_{22}-\lambda)(A_{33}-\lambda)(A_{44}-\lambda)(A_{55}-\lambda)(A_{66}-\lambda)=0 \tag{65}$$

Where,

$$\left.\begin{aligned}
&\lambda_1 = A_{11} = k_1 = -\left(\frac{1-\varepsilon}{\sigma_0}+\frac{\varepsilon}{\sigma_3}+\frac{1}{\mu_0}\right), \lambda_2 = A_{22} = k_5 = -\left(\frac{1-\theta}{\sigma_3}+\frac{\theta}{\sigma_1}+\frac{1}{\mu_0}\right),\\
&\lambda_3 = A_{33} = -\left(\frac{k_6k_9-k_5k_{10}}{k_5}\right), \lambda_4 = A_{44} = -\left(\frac{A_{34}k_{11}-A_{33}k_{12}}{A_{33}}\right),\\
&\lambda_5 = A_{55} = -\left(\frac{A_{45}B_1-A_{44}B_0}{A_{44}}\right), \lambda_6 = A_{66} = -\left(\frac{A_{56}B_7-A_{55}B_6}{A_{55}}\right).
\end{aligned}\right\} \tag{66}$$

This means that all the eigenvalues of the characteristic equation (65) have negative real parts and, therefore, E_0 is stable. This implies that,

$$\frac{(1-\theta)Q_0}{\alpha_0\sigma_1\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)}+\frac{(1-\theta)(1-\nu)Q_0}{\delta(1-p)\sigma_1\sigma_2\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)\left(\frac{1}{\tau+p}+\frac{1}{\mu_0+\mu_1}\right)}<1 \tag{67}$$

$$R_{eff}<1 \tag{68}$$

4.2 Global Stability of Disease Free Equilibrium (DFE), E_0

Theorem 4.2. The DFE, E_0 of the model system is globally asymptotically stable if $R_{eff} \le 1$.

Proof.

We start by considering the Lyapunov-Laselle function [12].

$$V(S,L,B,I,Q,T)=\frac{GFL}{k_8}+\frac{HXB}{k_{12}}+\frac{HIk_{10}}{k_{12}} \tag{69}$$

Where,

$$\left.\begin{aligned}
&F=(1-\theta)Q_0, G=[1+(1-\nu)], X=(1-k_{11}),\\
&H=[\alpha_0+\delta(1-p)\sigma_2k_{12}]\sigma_1k_5
\end{aligned}\right\} \tag{70}$$

Differentiating (69), we have:

$$\frac{dV}{dt}=\frac{GF}{k_8}[k_4S+(k_7I+k_6B+k_8)Q+k_5L]+\frac{HX}{k_{12}}[k_9L+k_{10}B]+\frac{Hk_{10}}{k_{12}}[k_{11}B+k_{12}I] \tag{71}$$

Since

$$S\le S_0, L\le L_0, B\le B_0, I\le I_0, Q\le Q_0 \ \&\ T\le T_0 \tag{72}$$

Equation (70) becomes

$$\frac{dV}{dt}\le\left(\frac{k_4S_0+k_8Q_0}{k_8}\right)\left[\frac{(1-\theta)Q_0}{\alpha_0\sigma_1\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)}+\frac{(1-\theta)(1-\nu)Q_0}{\delta(1-p)\sigma_1\sigma_2\left(\frac{\theta}{\sigma_3}+\frac{1-\theta}{\sigma_1}+\frac{1}{\mu_0}\right)\left(\frac{\nu}{\sigma_3}+\frac{1-\nu}{\sigma_2}+\frac{1}{\mu_0}\right)\left(\frac{1}{\tau+p}+\frac{1}{\mu_0+\mu_1}\right)}-1\right] \tag{73}$$

$$= \left(\frac{k_4 S_0 + k_8 Q_0}{k_8} \right) \left[R_{eff} - 1 \right] \quad (74)$$

Then, clearly $\frac{dV}{dt} \leq 0$ (75)

if $R_{eff} \leq 1$ (76)

Hence, the DFE is globally asymptotically stable.

4.3 Graphical Representation of Effective Reproduction Number with Control Variables

In this section, we compute numerical simulations and vary the control parameters with the effective reproduction number, R_{eff}. The control parameters are drug therapy and treatment rate where k is the different proportion of each control parameters.

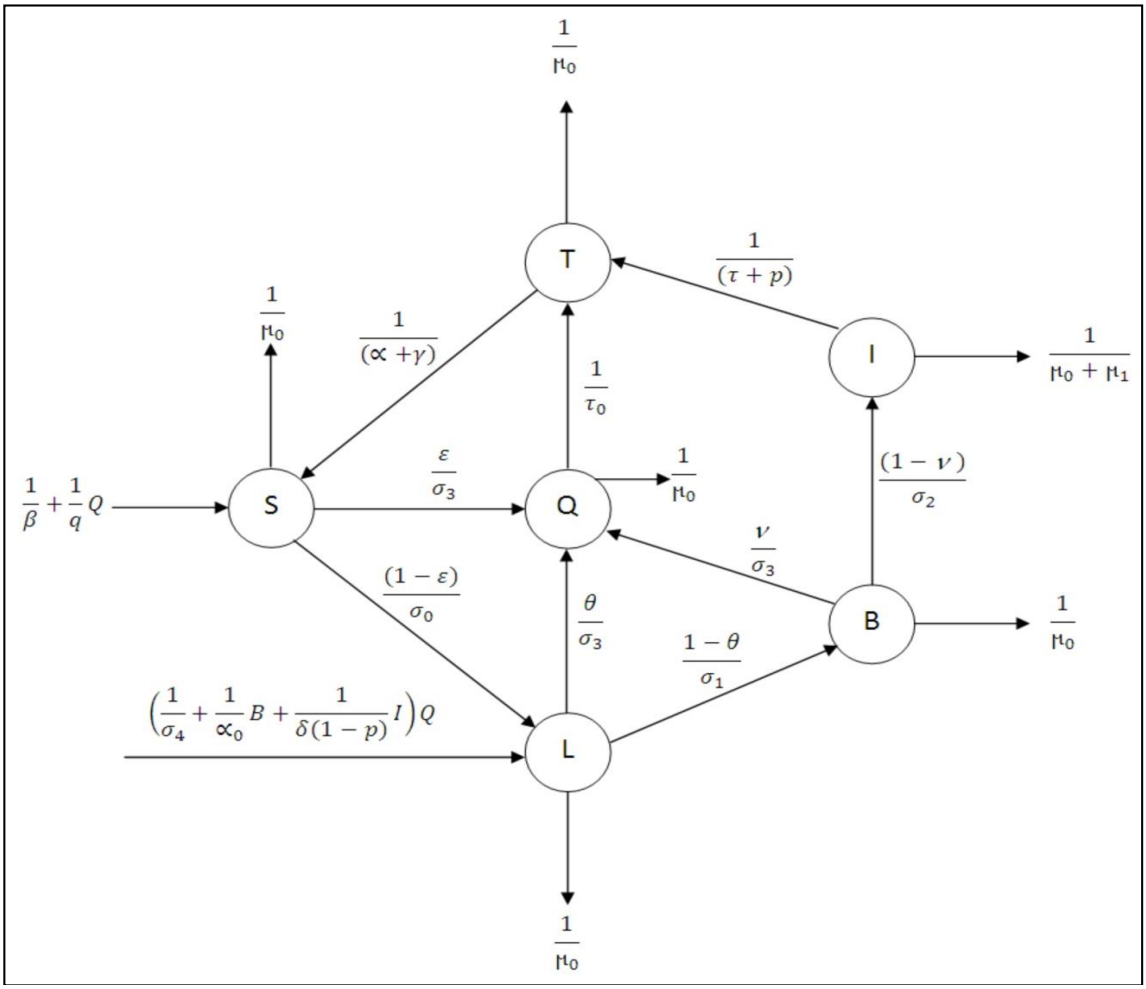

Fig 1: Model flowchart

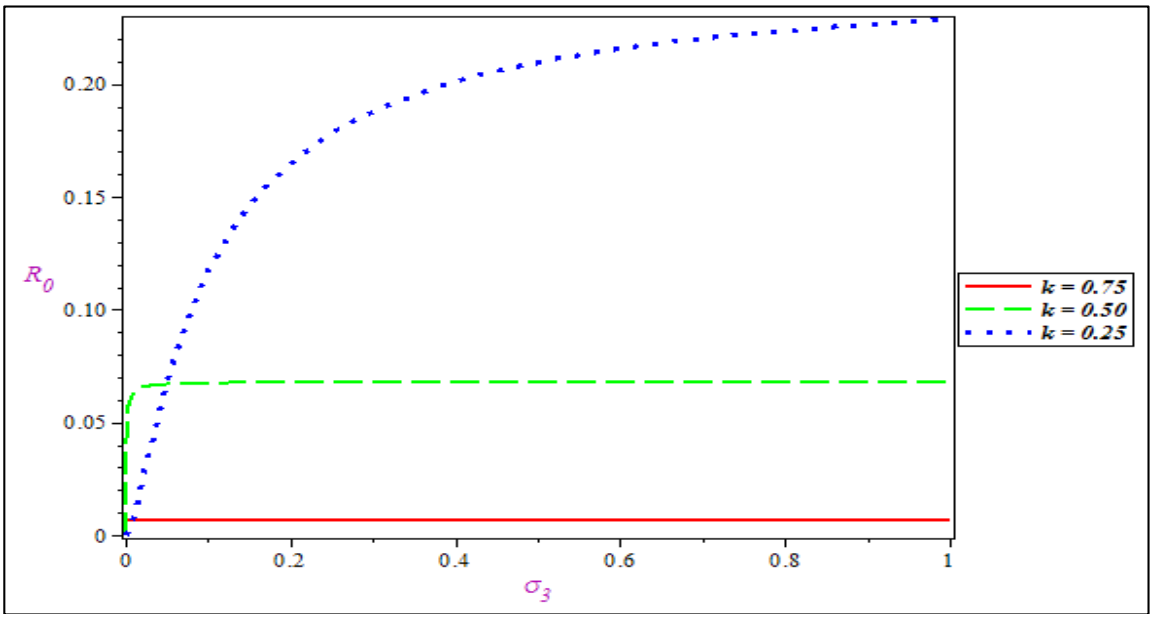

Fig 2: Effect of time to seek drug therapy on effective reproduction number.

Figure 2, shows that, as time to seek drug therapy increases the effective reproduction number decreases. This implies that placing individuals on a regular anti-malaria therapy where malaria disease is endemic will reduce the numbers of malaria patients in the hospitals. The availability of anti-malaria and time to seek the therapy is a practical key in controlling malaria disease in sub-Sahara African regions that are endemic with malaria.

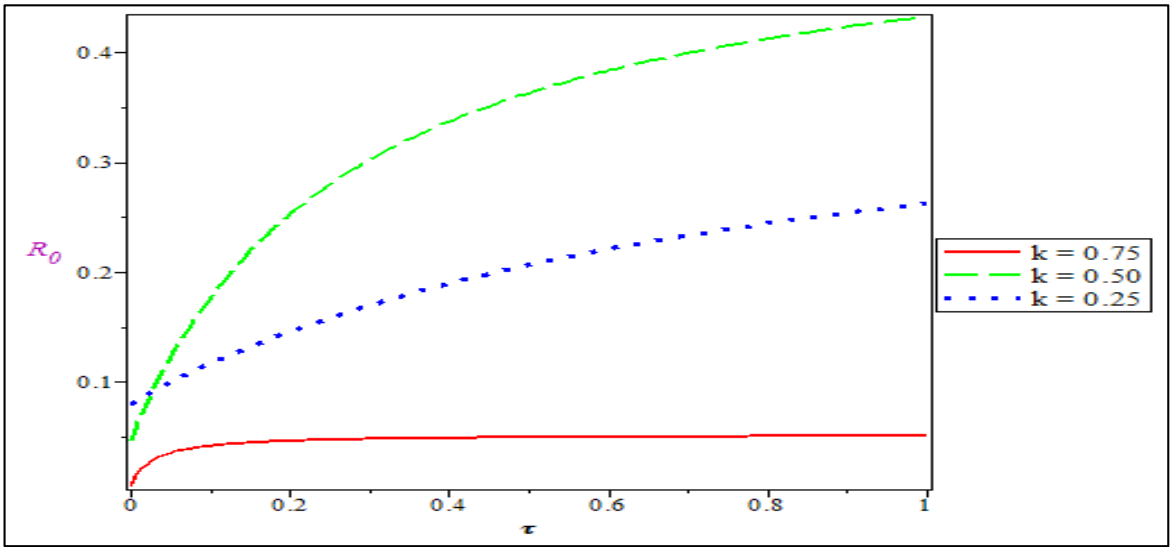

Fig 3: Effect of time to seek treatment on effective reproduction number.

Figure 3 illustrates the effect of time to seek treatment, as the treatment rate increases the effective reproduction number decreases with time. Having access to malaria treatment facilities in the sub-Sahara African communities where malaria is an endemic disease will drastically reduce malaria persistence.

5. Conclusion

We observed from all the analysis that the local and global stability of Disease Free Equilibrium (DFE) is asymptotically stable if $R_{eff} < 1$ and $R_{eff} \leq 1$, respectively. The implication here is, once the malaria disease breaks out in a population it can die out with time. Since the effective reproduction number is either less than or equal to one for local and global stability respectively. The numerical simulation as demonstrated by figures two and three showed that if the time to seek ant-malaria drug therapy is regular, availability of drug therapy, time to seek treatment and accessibility of malaria treatment facility are put together in the community, this will bring malaria disease under control. We also observed from all the graphs that the effective reproduction number is less than one which implies that the malaria disease will not persist in the population if all the control measures are being implemented into national health policy.

Government at all levels should ensure that anti-malaria drug therapies and treatment facilities are always accessible to people; and individuals should also be sensitized to avoid mosquitoes bite.

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