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Mathematical Approach for Modelling Malaria Disease in the Presence of Drug Therapy and Treatment

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Abstract: An $S-L-B-I-Q-T$ epidemic mathematical model incorporating drug therapy and treatment is investigated for malaria disease. We obtained the Disease Free Equilibrium (DFE) points and compute the basic reproduction number (R_0). The local and global stability of the Disease Free Equilibrium was analyzed using Jacobian matrix stability techniques and Lyapunov function respectively. The local and global stability was asymptotically stable if $R_0 < 1$ and $R_0 \leq 1$ respectively. Sensitivity analysis of R_0 for drug therapy and treatment showed that R_0 is strictly a decreasing function of σ_3, θ, v, τ and p. The numerical simulation of R_0 and control parameters of the model were presented graphically. The findings of this study strongly suggest a combination of effective drug therapy and treatment as a crucial strategy to control the malaria disease.

Keywords: Malaria disease, Drug therapy, Treatment, Sensitivity, Stability.

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 [3] the authors proposed a mathematical model and compared their model to an alternate version of the SLBI model. In their formulation, the probability of receiving treatment$p$is applied at the time of acquiring infection rather than the time of

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infection, as an alternative way of capturing the proportion of infections that are treated. They also assumed that since there is no treatment compartment explicitly, the total time to move from being infectious to becoming susceptible again is ($q + \tau$) and hence the population who receive drug therapy with probability q do so at a rate of $p \times 1/(q + \tau)$. The populations that are infectious but remain untreated recovered naturally at the natural recovery rate ($(1 - p)/\delta$). However, as pointed out by World Health Organization ([4, 5]) 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.

In our paper, we incorporate compartments of drug therapy and treatment where 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. Our model is a holistic approach to real life situation in that we incorporate demography and malaria caused death. We also allow the reproduction rate of malaria virus from the mosquitoes to enter the model. Hence, susceptible individuals are allowed to be either under drug therapy or latent with certain probabilities.

The organization of this paper is as follows: The model equations are formulated in section 2. Section 3 is concerned with deriving the basic reproduction number and sensitivity analysis on basic reproduction number. Local and global stability analysis of disease free equilibrium and numerical simulation were obtained in section 4. The discussion of the work is presented in section 5. Recommendations and suggestion for further studies are presented in section 6 in the form of concluding remarks.

2. Formulation of the Model Equations

2.1. The Existing Model

We begin our model formulation by introducing the model of [3]; we first present the parameters and assumptions of the existing model.

2.2. Assumptions of the Existing Model

The following are the assumptions of the existing model by [3]

(i). 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.

(ii). The natural recovery period is assumed to be longer than the drug recovery period and the time to infectiousness.

(iii). Natural recovery is only possible once the disease is at the infectious stage and not any earlier.

(iv). Probability of receiving treatment p is applied at the time of acquiring infection rather than during the infection, and those who do not receive drug therapy recovered naturally.

(v). Birth, death, super-infection and the development of immunity through repeated infections are ignored.

2.3. Variables and Parameters of the Existing Model

Table 1 shows definition of variables and parameters of the existing model.

	s Description
$S(t)$	Susceptible individuals at time t
$L(t)$	Latent period at time t
$B(t)$	Symptomatic individuals at time t
$I(t)$	Infected period at time t
σ_1	Period of latent
σ_2	Time of infectiousness
τ	Time to seek treatment
q	Drug recovery period
δ	Natural recovery period
p	Probability of treatment
λ	Force of infection
N	Population size
t	Time

Table 1.

The following is a flow diagram of the existing model.

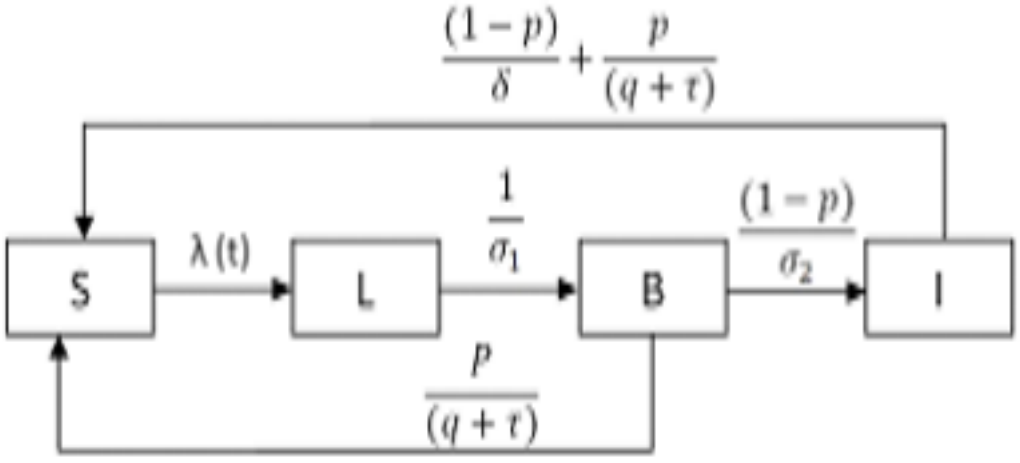

Figure 1. Flow diagram of malaria for the existing model

2.4. The Equations of the Existing Model

Using the above assumptions, parameters and flow diagram, [3] derived the following model equations.

$$dt = -\lambda(t)S + (1 - p)$$

$$dS$$

$$\delta I + p$$

$$(q + \tau)(B + I) \quad (1)$$

$$\frac{dL}{dt} = \lambda(t)S - {}^{1}\sigma_1 L \quad (2)$$

$$\frac{dB}{dt} = {}^{1}\sigma_1 L - (1-p)\sigma_{2B} - p(q+\tau)B \quad (3)$$

$$\frac{dI}{dt} = (1-p)\sigma_{2B} - (1-p)\delta I - p(q+\tau)I \quad (4)$$

2.5. The Extended Model

We shall use the following assumptions and flow diagram to derive the extended model used in this work.

2.6. Assumptions of the Extended Model

In addition to the assumptions by [3] we make the following assumptions:

(i). The population N is compartmentalized into the proportions of susceptible individuals $S(t)$, proportions of latent individuals $L(t)$, proportions of symptomatic individuals $B(t)$, proportions of infected individuals $I(t)$, proportions of drug therapy class $Q(t)$, and proportions of treatment class $T(t)$.

(ii). The classes $S(t)$, $L(t)$ and $B(t)$ seek drug therapy at a regular rate σ_3.

(iii). 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.

(iv). Time to seek treatment after drug therapy is not equal time to seek treatment during infection (v). Becoming susceptible again is the combined effects of treatment drug therapy and recovery rate per infected individual. (vi). Reproduction rate of malaria virus and death removal rate are not equal.

(vii). Disease induce death rate is applicable to only infected class $I(t)$.

(viii). We ignored natural recovery and assumed that drug therapy alone is not sufficient enough to cure malaria.

(ix). Probability of receiving treatment p is applied during the infection, and those who recovered naturally δ without drug and treatment moved into $L(t)$, we assumed the malaria virus is not cleared in their body.

2.7. Variables and Parameters of the Extended Model

Table 2 shows definition of variables and parameters of the extended model

	s Description
$Q(t)$	Drug therapy period at time t
$T(t)$	Treatment period at time t
σ_0	Period of susceptible
σ_3	Time to seek drug therapy
σ_4	Latent period after drug therapy
τ_0	Time to seek treatment after drug therapy

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
v	Symptomatic proportions that seek drug therapy at σ_3
$\delta(1-p)$	Rate of moving from infected to latent when there is no drug therapy and treatment

Table 2.

The flow diagram for the existing model is amended to obtain the flow diagram for the extended model as follows.

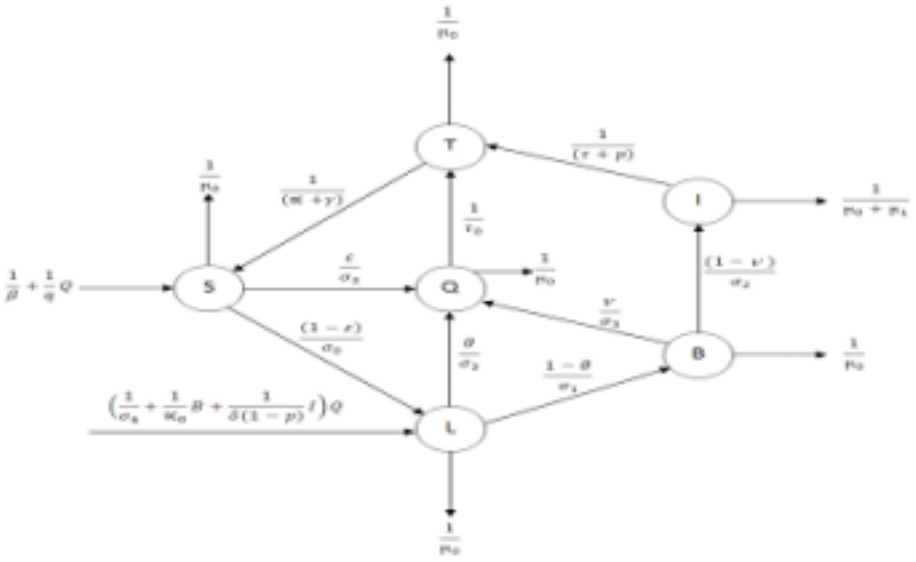

Figure 2. Flow diagram of malaria for the extended model

2.8. Equations of the Extended Model

The proportions of drug therapy $Q(t)$ and treatment class $T(t)$ are incorporated into the extended model explicitly as shown in equations (9) to (11). In the expanded model, we consider the influx of malaria virus reproduction at a rate β, equal natural death which is applicable to all the compartments at a rate μ_0, disease induce death only to infectious class at a rate μ_1 and

latent rate α_0 relative to infection by symptomatic class $B(t)$. Also, time to seek drug therapy σ_3, treatment rate α, and recovery rate γ are incorporated in the model equations. Based on the above assumptions, Variables, parameters and flow diagram, we extend the model by [3] as follows

$$\frac{dS}{dt} = \left(\frac{1}{\beta} + \frac{1}{qQ} + 1\right) \quad \frac{dL}{1-\varepsilon} \quad \sigma_0 + \frac{\varepsilon}{\sigma_3} + \frac{1}{\mu_0 S} \quad (5)$$

$$\frac{dT}{dt} = (\alpha + \gamma)T - \quad - \theta \quad 1$$

$$\frac{dL}{dt} = 1 - \varepsilon \quad \delta(1-p)I + \frac{1}{\alpha_0 B} + \frac{1}{\sigma_4 Q} - \frac{\theta}{\sigma_3} + 1 \quad \sigma_0 S + \quad \frac{1}{(\mu_0 + \mu_1)}$$

$$\sigma_1 + \frac{1}{\mu_0 L} \quad (6) \qquad \sigma_3 + 1 - v \qquad I \quad (8)$$

$$\frac{dB}{dt} = 1 - \theta \quad \sigma_1 L - \quad \sigma_2 B - \quad \frac{dQ}{dt} = \frac{1}{\sigma_3}(\varepsilon S + \theta L + vB) - \frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0 Q} \quad (9)$$

$$\sigma_2 + \frac{1}{\mu_0 B} \quad (7) \qquad v \qquad (\tau + p) + 1$$

$$\frac{dI}{dt} = 1 - v$$

$$\frac{dT}{dt} = 1 \quad (\tau + p)I + \frac{1}{\tau_0 Q} - 1 \quad (\alpha + \gamma) + \frac{1}{\mu_0 T} \quad (10)$$

$S(0) \geq 0$, $L(0) \geq 0$, $B(0) \geq 0$, $I(0) \geq 0$, $Q(0) \geq 0$, $T(0) \geq 0$. Because the extended model is in terms of proportions, $S(t) + L(t) +$

$$B(t) + I(t) + Q(t) + T(t) = 1 \quad (11)$$

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

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

3. The Basic Reproduction Number, R_0

We now calculate the disease-free equilibrium state of the extended model. We begin this by setting the left hand sides of equations (5) to (11) to zero and get the disease-free equilibrium state as follows. The disease-free equilibrium state, $E_0 = (S_0, 0, 0, 0, Q_0, T_0)$. Where,

$$S_0 = \quad \frac{\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}}{1-\varepsilon + \frac{\varepsilon\sigma_3}{} + \frac{1\mu_0}{} \frac{1}{q} + \frac{1\tau_0}{} + \frac{1\sigma_4}{} + \frac{1\mu_0}{}\sigma_3 \frac{1}{}} \quad \sigma_3 \quad (12)$$

$$\beta \qquad \varepsilon - \frac{1}{\alpha+\gamma + \frac{1\mu_0}{}} - \frac{1}{q} \frac{1}{}$$

$$Q_0 = 1 \quad \frac{(\alpha+\gamma)\tau_0}{1-\varepsilon + \frac{\varepsilon\sigma_3}{} + \frac{1\mu_0}{} \frac{1}{q} + \frac{1\tau_0}{} + \frac{1\sigma_4}{} + \frac{1\mu_0}{}\sigma_3} \quad \varepsilon \quad (13)$$

$$\frac{1}{} \qquad \varepsilon - \frac{1}{}$$

$$T_0 = \frac{\beta}{\alpha+\gamma+\frac{1}{\mu_0}(14)\,1}$$

Remark 3.1. *For SEIR models, the rate of appearance of new infections is given by the new infection terms in the latent compartment [6–8].*

From the equations (5) to (11) of the expanded model, we have the following:

The vector $F(x)$ of the rates of new infections in compartments $L(t)$, $B(t)$ and $I(t)$ is given by

$$F(x) = \begin{bmatrix} \sigma_0 S + \\ 0 \\ \delta(1-p)I + \frac{1}{\alpha_0}B + \frac{1}{\sigma_4}\frac{1}{Q} \\ 0 \end{bmatrix} \quad (15)$$

Also, the remaining transfer terms in compartments L, B and $I$is given by equation (16).

$$V(x) = \begin{bmatrix} \sigma_3 + \frac{1-\theta}{\theta} \\ -\frac{1-\theta}{\theta}\sigma_1 L + \sigma_1 + \frac{1}{\mu_0}\sigma_3 + \frac{1-\nu}{\nu} L \\ -\frac{1-\nu}{\nu}\sigma_2 B + \sigma_2 + \frac{1}{\mu_0} B \\ -\frac{1}{(\tau+p)} + \frac{1}{(\mu_0+\mu_1)} I \end{bmatrix} \quad (16)$$

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

$$F_x(E_0) = \begin{bmatrix} 0 & \frac{1}{\alpha_0}Q_0 & 0 \\ \delta(1-p)Q_0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad (17)$$

$$Q_0 = \frac{1}{1-\varepsilon + \frac{\varepsilon\sigma_3}{1} + \frac{1}{\mu_0}\frac{1}{q} + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}\sigma_3} \quad (18)$$

$$\beta \qquad (\alpha+\gamma)\tau_0 \qquad \frac{\varepsilon}{\alpha+\gamma+\frac{1}{\mu_0}-\frac{1}{q}\,1}$$

And the matrix of partial derivatives of $V(x)$at DFE State $\bar{x} = \sigma_1 + \frac{1}{\mu_0} 0\ 0$ $E_0 = (S_0, 0, 0, 0, Q_0, T_0)$ is

$$V_x(E_0) = \begin{bmatrix} \frac{\theta}{\sigma_3 + \frac{1-\theta}{\theta}} \\ -\frac{1-\theta}{\theta} & \sigma_3 + \frac{1-\nu}{\nu} \\ \frac{\nu}{\sigma_1} & \sigma_2 + \frac{1}{\mu_0} 0 \\ 0 \quad -\frac{1-\nu}{\nu}\sigma_2 & \mu_0+\mu_1 \\ \frac{1}{\tau+p} + \frac{1}{1} \end{bmatrix} \quad (19)$$

It follows that the basic reproduction number R_0 is given by equation (20).

$$R_0 = \rho F_x V^{-1} \quad (20)$$

$$R_0 = (1-\theta)Q_0 \frac{\alpha_0\sigma_1}{\sigma_1 + \frac{1}{\mu_0}} \frac{\theta}{\sigma_3 + \frac{1-\theta}{\sigma_1 + \frac{1}{\mu_0}}} \frac{\nu}{\sigma_3 + \frac{1-\nu}{\sigma_2 + \frac{1}{\mu_0}}} + (1-\theta)(1-\nu)Q_0 \frac{\delta(1-p)\sigma_1\sigma_2}{\sigma_2 + \frac{1}{\mu_0}} \frac{\theta}{\sigma_3 + \frac{1-\theta}{\sigma_1 + \frac{1}{\mu_0}}} \frac{\nu}{\sigma_3 + \frac{1-\nu}{\sigma_2 + \frac{1}{\mu_0}}} \frac{\tau+p+\frac{1}{1}}{\mu_0+\mu_1} \quad (21)$$

Theorem 3.2. *R_0 is a strictly decreasing function of σ_3, θ, τ, ν, $p \in (0, 1)$.* ***Proof.*** The partial derivative of R_0 with respect to σ_3, θ, τ, $\nu$and $p$is given by (22)-(26).

$$\frac{\partial R_0}{\partial \sigma_3} = - \quad < 0 \quad (22)$$

$$\frac{\partial R_0}{\partial \theta} = - \quad < 0 \quad (23)$$

$$\frac{\partial R_0}{\partial \tau} = -\tau Q_0((1-\theta)(1-\nu)) \quad < 0 \quad (24)$$

4. Result

4.1. Local Stability Analysis of the Disease-Free Equilibrium (DFE), E_0

Theorem 4.1. *The Disease-Free Equilibrium of the model system* (5)-(10) *is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

Proof. We shall first compute the Jacobian matrix for the DFEs using equations (5) - (10). The Jacobian matrix for the disease-free state J_{E_0} is given as

$J_{E_0} =$ $\sigma_1 -$ v $\sigma_2 + 1 \mu_0$ 0 0

0 0 $1-v$ $\sigma_2 -$ $\tau+p$ $+1$ $\frac{1}{\mu_0+\mu_1}$

$\frac{\varepsilon}{\sigma_3}$ $\frac{\theta}{\sigma_3}$ $\frac{v}{\sigma_3}$ 0 $-$ $q + \frac{1}{\tau_0} + \frac{1}{\sigma_4} + \frac{1}{\mu_0}$ 1 0

0 0 0 1 $\tau+p$ $\frac{1}{\tau_0} -$ $\alpha+\gamma$ $+ \frac{1}{\mu_0}$ 1

For ease of analysis, we perform the following operations on equation (27) and obtain (28).

$k_{13}\ k_{14}\ k_{15}\ 0\ k_{16}\ 0\ 0\ 0\ 0\ k_{17}\ k_{18}\ k_{19}$

$J_{E_0} =$ (28)

Where,

$k_1\ 0\ 0\ 0\ k_2\ k_3$

$k_4\ k_5\ k_6\ k_7\ k_8\ 0\ 0\ k_9\ k_{10}\ 0\ 0\ 0\ 0\ 0\ k_{11}\ k_{12}\ 0\ 0$

$k_1 = A_{11} = -$ $\sigma_0,$ $, k_6 = A_{23} = \frac{Q}{\alpha_0}$, $k_7 = A_{24} = \frac{Q}{0}$

$k_5 = A_{22} = -$ $\sigma_3 + \frac{\theta}{} \sigma_1 + \frac{1}{} \mu_0\ \underline{1-\theta}$

$\sigma_0 + \frac{\varepsilon}{} \sigma_3 + \frac{1}{} \mu_0$ $\underline{1-\varepsilon}$, $k_2 = A_{15} = \frac{1}{q}$, $k_3 = A_{16} = \frac{1}{}$

$\alpha+\gamma$, $k_4 = \underline{1-\varepsilon}$ $\delta(1-p)$, $k_8 = \frac{1}{} \sigma_4$,

$k_9 = \underline{1-\theta}$ $\sigma_2 + \frac{v}{} \sigma_3 + \frac{1}{} \mu_0$ σ_2, $k_{12} = -$ $\frac{1}{\mu_0+\mu_1}$ (29) ,

σ_1, $k_{10} = -$

$\underline{1-v}$, $k_{11} = \underline{1-v}$ $\tau+p$ $+1$

$k_{13} = \frac{\varepsilon}{} \sigma_3$, $k_{14} = \frac{\theta}{} \sigma_3$, $k_{15} = \frac{v}{} \sigma_3$, $q + \frac{1}{} \tau_0 + \frac{1}{} \sigma_4 + \frac{1}{} \mu_0\ 1$, $k_{17} = \frac{1}{} \tau+p$,

$k_{16} = -$

$k_{18} = \frac{1}{} \tau_0$, $k_{18} = -$ $\alpha+\gamma$ $+ \frac{1}{} \mu_0\ 1$

Using Gaussian elimination row operation on the equation (28), we obtain the following

$A_{11} - \lambda\ 0\ 0\ 0\ A_{15}\ A_{16}$

$0\ A_{22} - \lambda\ A_{23}\ A_{24}\ A_{25}\ A_{26}$

$M =$ (30)

k_1, $A_{26} = -\frac{k_3 k_4}{}$

Where,

$0\ 0\ A_{33} - \lambda\ A_{34}\ A_{35}\ A_{36}\ 0\ 0\ 0\ A_{44} - \lambda\ A_{45}\ A_{46}\ 0\ 0\ 0\ 0$

$A_{55} - \lambda\ A_{56}\ 0\ 0\ 0\ 0\ 0\ A_{66} - \lambda$

k_1, $A_{33} = \frac{k_5 k_{10} - k_6 k_9}{}$

$A_{25} = \frac{k_1 k_8 - k_2 k_4}{}$ k_5, $A_{36} = -\frac{A_{26} k_9}{}$

$A_{35} = -\frac{A_{25} k_9}{}$ k_5, $A_{34} = -\frac{k_7 k_9}{} k_5$,

□□□□□□□□□(31)

k_5, $A_{44} = \frac{A}{33}\frac{k_{12}}{k_{12}} - \frac{A_{34}k_{11}}{}$
A_{33}, $A_{45} = -\frac{A}{35}\frac{k_{11}}{}$
A_{33},
$A_{46} = -\frac{A}{36}\frac{k_{11}}{}$
A_{33}, $A_{55} = \frac{A}{44}\frac{B_0}{} - \frac{A_{45}B_1}{}$
A_{44}, $A_{56} = \frac{A}{44}\frac{B_5}{} - \frac{A_{46}B_1}{}$

A_{44},
$A_{66} = \frac{A}{55}\frac{B_6}{} - \frac{A_{56}B_7}{}$
A_{55}

To simplify the notations, we let

$B_0 = \frac{A}{33}\frac{B_2}{} - \frac{A_{35}B_3}{}$
A_{33}, $B_1 = \frac{A}{33}\frac{B_4}{} - \frac{A_{34}B_3}{}$

A_{33}, $B_2 = \frac{B}{8}\frac{k_5}{} - \frac{A_{25}k_{14}}{}$
k_5,
$B_3 = \frac{k}{5}\frac{k_{15}}{} - \frac{k_6k_{14}}{}$
k_5, $B_4 = -\frac{k}{7}\frac{k_{14}}{}$

k_5, $B_5 = \frac{A}{33}\frac{B_3}{} - \frac{A_{36}B_3}{}$
A_{33},
$B_6 = \frac{A}{44}\frac{k_{19}}{} - \frac{A_{46}k_{17}}{}$
A_{44}, $B_7 = \frac{A}{44}\frac{k_{18}}{} - \frac{A_{45}k_{17}}{}$

A_{44}, $B_8 = \frac{k}{1}\frac{k_{16}}{} - \frac{k_2k_{13}}{}$

k_1,
$B_9 = -\frac{B}{10}\frac{k_5}{} - \frac{A_{26}k_{14}}{}$
k_5, $B_{10} = -\frac{k}{3}\frac{k_{13}}{}$

k_1

Therefore, the corresponding characteristic equation to Mas defined by equation (30) yield:

□□□□□□□□□
□□□□□□□□(32)

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

□□□□□□

$\lambda_1 = A_{11} = k_1 = -\frac{\sigma_0 + \varepsilon\sigma_3 + \frac{1}{\mu_0}}{1-\varepsilon}$, $\lambda_2 = A_{22} = k_5 = -\frac{1-\theta}{\sigma_3 + \theta\sigma_1 + \frac{1}{\mu_0}}$,

$\lambda_3 = A_{33} = -\frac{k_6k_9 - k_5k_{10}}{k_5}$, $\lambda_4 = A_{44} = -\frac{A_{34}k_{11} - A_{33}k_{12}}{A_{33}}$, □□□□□(34)

$\lambda_5 = A_{55} = -\frac{A_{45}B_1 - A_{44}B_0}{A_{44}}$, $\lambda_6 = A_{66} = -\frac{A_{56}B_7 - A_{55}B_6}{A_{55}}$.

This means that all the eigenvalues of the characteristic equation (33) have negative real parts and, therefore, E_0 is stable.

This implies that,

$$\frac{(1-\theta)Q_0}{\sigma_3 + \frac{1-\theta}{\sigma_1 + \frac{1}{\mu_0}}} + \frac{(1-\theta)(1-v)Q_0}{\sigma_3 + \frac{1-v}{}} < 1 \quad (35)$$

$\frac{v}{\sigma_2+\frac{1}{\mu_0}}$ $\sigma_3+\frac{1-\theta}{}$ $\sigma_1+\frac{1}{\mu_0}$ $\sigma_3+\frac{1-v}{}$

$\alpha_0\sigma_1$ $\delta(1-p)\sigma_1\sigma_2$ $\sigma_2+\frac{1}{\mu_0}$ $\mu_0+\mu_1$ $R_0 < 1$ (36)

$\frac{\theta}{v}$ $\frac{\theta}{v}$ $\tau+p+\frac{1}{1}$

4.2. Global Stability Analysis of the Disease-Free Equilibrium (DFE), E_0 Theorem 4.2.

The DFE, E_0 of the model system is globally asymptotically stable if $R_0 \leq 1$. Proof. We start by considering the Lyapunov-Laselle function [9].

k_8+HXB

$V(S, L, B, I, Q, T) = GF\,L$ (38)

Where, Differentiating (37) gives:

$F = (1-\theta)Q_0$, $G = [1 + (1-v)]$, $X = (1-k_{11})$, $H = [\alpha_0 + \delta(1-p)\sigma_2 k_{12}]\,\sigma_1 k_5$

$k_{12}+HIk_{10}$

k_{12} (37)

$k_8[k_4S + (k_7I + k_6B + k_8)\,Q + k_5L] + HX$

dV

$k_{12}[k_9L + k_{10}B] + Hk_{10}$
$k_{12}[k_{11}B + k_{12}I]$ (39)

$S \leq S_0$, $L \leq L_0$, $B \leq B_0$, $I \leq I_0$, $Q \leq Q_0$ *and* $T \leq T_0$ (40)

$dt = GF$

Since

$k_4S_0 + k_8Q_0$ (41)

Equation (39) becomes dV $(1-\theta)Q_0\,\theta\sigma_{3+}\frac{1-\theta}{}$

$dt \leq$ $\sigma_{1+}\frac{1}{\mu_0}\frac{v}{\sigma_{3+}}\frac{1-v}{}$ $\sigma_{2+}\frac{1}{\mu_0}$

$\alpha_0\sigma_1$

k_8 $+(1-\theta)(1-v)Q_0\,\theta\sigma_{3+}\frac{1-\theta}{}$ $\sigma_{1+}\frac{1}{\mu_0}\frac{v}{\sigma_{3+}}\frac{1-v}{}$ -1

$\delta(1-p)\sigma_1\sigma_2$ $\tau+p+\frac{1}{\mu_0+\mu_1}$

$\sigma_{2+}\frac{1}{\mu_0}1$

if

$[R_0 - 1]$ (42)
=

Then, clearly

$R_0 \leq 1$ (44)
$k_4S_0 + k_8Q_0\,k_8$

dV

$dt \leq 0$ (43)

Hence, the DFE is globally asymptotically stable.

□

4.3. Graphical Representation of Basic Reproduction Number with Control Param eters

We simulated the control parameters in the model with basic reproduction number. The control parameters are drug therapy and treatment rate. Where *k* is the different proportion of each control parameters.

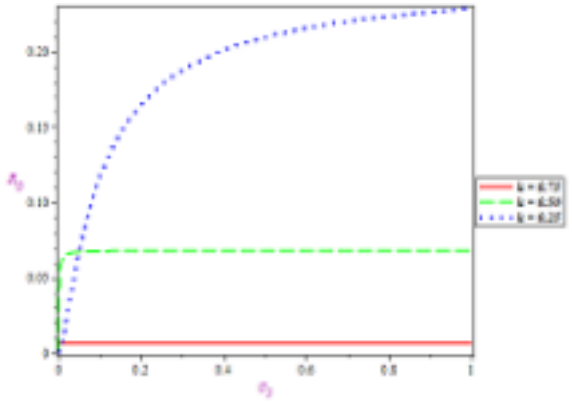

Figure 3. Effect of time to seek drug therapy

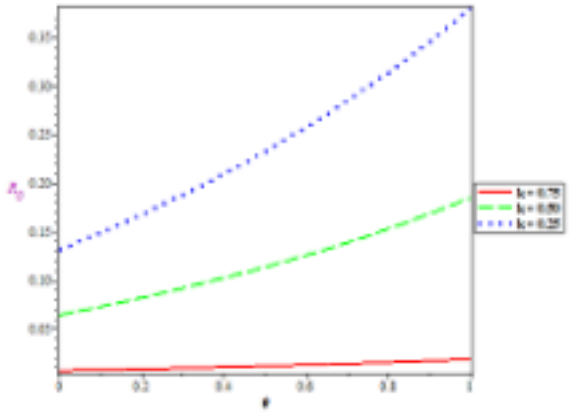

Figure 4. Effect of latent proportions to seek drug therapy

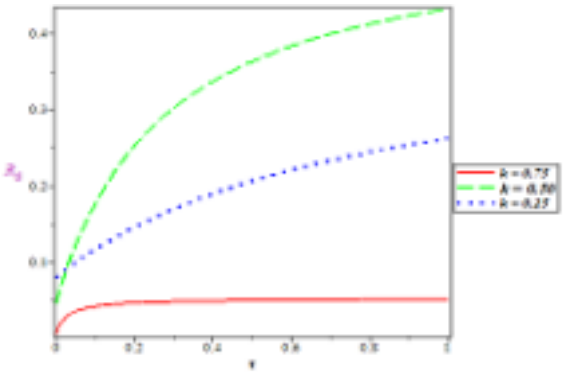

Figure 5. Effect of time to seek treatment

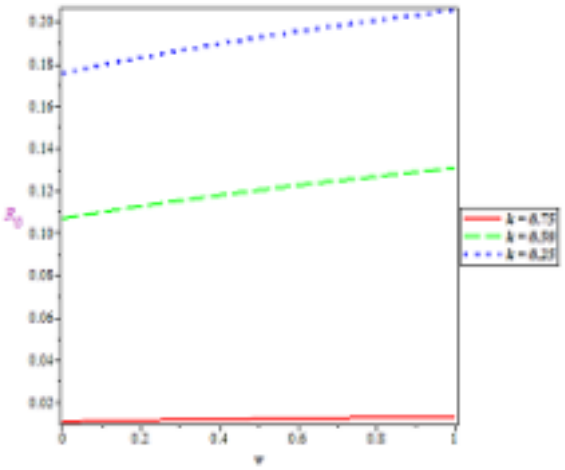

Figure 6. Symptomatic proportions that seek drug therapy

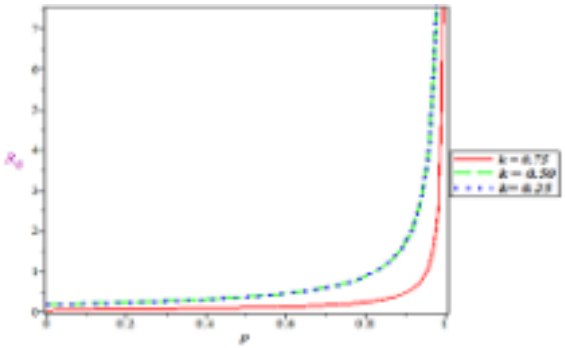

Figure 7. Effect of Probability of treatment

5. Discussion

We extended and analyzed a mathematical model of Malaria disease considering drug therapy and treatment as control measures. In the model analysis, we obtained R_0 and it serves as a threshold parameter that predicts whether the Malaria disease can spread in a susceptible population or not. The R_0 is to be used as a means of guide to the public health agencies on the amount of effort needed to control or eradicate the Malaria disease. From equations (36) and (44) the local and

global stability of DFE is asymptotically stable if $R_0 < 1$ and if $R_0 \leq 1$ respectively. This implies that Malaria disease can die

out with time. The R_0 was analytically evaluated for its sensitivity of time to seek drug therapy by latent proportion, time to seek treatment, symptomatic proportion that seek drug therapy and Probability of treatment by infected individuals while figure 3, 4, 5, 6 and 7 are the graphical presentation of R_0 against σ_3, θ, τ, v and p when the control parameters were each estimated at 25, 50 and 75 percent respectively. Clearly, the analytical sensitivity given by equation (22) to (26) and numerical simulation proved that R_0 is a decreasing function of drug therapy and treatment. It was observed from all the graphs that R_0 is less than one (i.e. $R_0 < 1$). This intuitive reasoning agrees with equation (22) to (26) which gives possibility to put Malaria disease under control.

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