IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

Mathematical Analysis of Basic Reproduction Number for the Spread and Control of Malaria Model with Non-Drug Compliant Humans

T. S. Faniran [1*] And Ayoola E. O. [2]

1 *, Department of Computer and Physical Sciences, Lead City University, Ibadan, Nigeria.
2, Department of Mathematics, University of Ibadan, Ibadan, Nigeria.
Corresponding Author email: tayefaniran@yahoo.com

Article Info
Received: 12 June 2019 Revised: 2 September 2019
Accepted: 25 October 2019. Available online: 22 November 2019

Abstract

Malaria arises when there is an infection of a host by Plasmodium falciparum that causes malaria in humans. Non-drug compliance results from not taking medication as prescribed by doctors. Previous research had concentrated on mathematical modeling of transmission dynamics of malaria without considering some infectious humans who do not comply to drug. This study is therefore designed to model transmission dynamics of malaria taking into consideration some infectious humans who do not comply to drug. The model is formulated using nonlinear ordinary differential equations. The human population is partitioned into Susceptible human (S_H), Exposed Human E_H, Infectious human (I_H), Non-drug compliant human I_{NH} and Recovered human (R_H). Using next generation matrix, the reproduction number R_0 is obtained. This is used to analyse the global stability of the disease-free equilibria and local stability of the endemic equilibria of the model. The global stability of the disease-free equilibria and the local stability of the endemic equilibrium of the model are established through the construction of suitable Lyapunov function and analysis of characteristic equation. It is shown that the disease-free equilibrium is globally asymptotically stable whenever $R_o < 1$. It is also shown that the endemic equilibrium becomes stable through the Routh-Hurwitz stability criteria.

Keywords: Non-drug compliance, Basic reproduction number, Stability.
MSC2010:34C20. 22E30. 92D30

1 Introduction

Malaria is a complex parasitic disease. It is mostly confined to tropical and subtropical regions of Africa and Asia because of rainfall, warm temperatures, stagnant water and poor sanitation that pave way for the provision of conducive environment for mosquito breeding [1, 17, 16]. Although, there were tremendous progresses in the fight against malaria. According to the World Health

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

Organization's records for the year 2013, there were 207 million malaria cases worldwide with 627,000 deaths in 2012 [19, 25].

Malaria infection is characterized by high fever, chills, sweating, fatigue, headache and nausea. If it is left untreated, it can cause acute anemia, organ failure or brain damage among the problems. Malaria is common and life-threatening public health problem in many tropical and sub-tropical areas of the world. It is currently endemic in over hundred countries. Each year, approximated three hundred million people fall ill with malaria and one million deaths are recorded. It is transmitted by female anopheles mosquitoes who bite mainly between sunset and sunrise [3, 26].

Human malaria is caused by five different species of the parasite belonging to genius Plasmodium: Plasmodium falciparum (the most deadly), Plasmodium vivax, Plasmodium knowlesi, Plasmodium malariae and Plasmodium ovale. The last two are fairly uncommon. Plasmodium knowlesi causes malaria in animal but can also infect humans and may be fatal. Animal malaria does not spread to humans [11].

Malaria symptoms appear seven days or more (usually 7-15 days) after being bitten by infectious mosquitoes. Malaria is preventable and curable. It can be treated in just 48 hours through the use of Artemisinin-based Combination Therapy (ACT) with drug compliance. But it can result into complication if it is diagnosed and treated lately. It can be prevented by using insecticides, treated bed nets, spraying with residual insecticides e.t.c.

Over the years, mathematical modeling of the spread of malaria has become an important tool in understanding the transmission dynamics of the diseases, predicting and controlling the spread of malaria in the future. Bakary et al.,[5] formulated a mathematical model of non-autonomous ordinary differential equations describing the dynamics of malaria transmission with age structure for the vector population. They obtained the basic reproduction number, R_o and proved that the disease-free equilibrium is locally asymptotically stable for $R_o < 1$. They performed numerical simulations to illustrate their analytical results. They concluded that malaria transmission can be controlled by fighting against the proliferation of the mosquitoes namely, by reducing available breeder sites. Ousmane et al., [20] presented a mathematical model of malaria transmission by considering two models: a model of vector population and a model of virus transmission. They applied Lyapunov principle to study the stability of equilibrium points. They determined the basic reproduction number using the next generation matrix. Their numerical simulations revealed that malaria management is concerned firstly by lowering the mosquito threshold parameters to a value less than unity. Chitnis et al., [7] formulated a mathematical model for the spread of malaria in human and mosquito population where they found that the disease-free equilibrium is locally asymptotically stable when $R_o < 1$ and unstable when $R_o > 1$. Their numerical simulations showed that for larger values of the disease-induced death rate, a subcritical (backward) bifurcation is possible at $R_o = 1$. Wedajo et al., [24] formulated and analyzed SIR model of malaria that included infected immigrants. The reproduction number R_o of their model was calculated using the next generation matrix method. They established the global stability of the equilibrium points using the Lyapunov function and LaSalle Invariance Principle. They simulated their analytical results and concluded that the infected immigrants will contribute positively and increase the disease in the population.

We modified and extended a model developed by Wedajo et al., [24] by incorporating a new class of non-drug compliant human compartment into the human population. These are the people who are given medication by their doctors but do not take it as prescribed. These include those who fail to take the correct dosage and those who do not complete their medication, that is, those who stop taking their medication as soon as they think that they feel better after few days of starting treatment. Using stability theory of nonlinear ordinary differential equations, global dynamics of the model is analyzed. Also, local stability of the endemic equilibrium solution of the model is established.

In addition to the introductory section, the paper has three more sections. Section two shows the mathematical formulation of the model. In section three, transformation of the model is presented.

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

In section four, stability analysis of the model is carried out. Section five discusses the results and concludes the modeling work.

2 Materials and Methods

In this section, a model for the spread of malaria in the human population and mosquito vector population is formulated. A malaria model incorporating some infectious humans who do not comply with drug, is introduced. The total human population denoted by N_H is sub-divided into five classes namely; the susceptible humans S_H, the exposed humans E_H, the infectious humans I_H, the non-drug compliant humans I_{NH} and the recovered humans R_H so that $N_H = S_H + E_H + I_H + I_{NH} + R_H$. Also, the total mosquito vector population denoted by N_V, is sub-divided into two classes namely; the susceptible mosquito vector, S_V and the infected mosquito vector I_H. Thus the total population N_H and N_V for human and mosquito population is given by $N_H = S_H + E_H + I_H + I_{NH} + R_H$ and $N_V = S_V + I_V$.

2.1 Nomenclature/Values of Parameters Involved in the Model

a = average biting rate on man by a single mosquito (infection rate) 0.29 [10]
b = the proportion of bites on man that produces infection 0.75 [10]
p = probability that a mosquito becomes infected 0.75 [10]
θ= fraction of infectious who comply with drug 0.8 [Assumed]
$(1-\theta)\tau$= fraction of infectious who do not comply with drug 0.2 [Assumed]
τ = drug efficacy 0.01-0.7 [Assumed]
δ = death rate due to malaria 0.333 [22]
μ_N = death due to non-drug compliance 0.05 [Assumed]
ν = recovery rate 0.0022 [9]
π_h = natural birth rate of humans 0.0015875 [9]
π_v = natural birth rate of mosquitoes 0.071 [9]
α = progression rate of exposed humans 0.0588 [6]
μ_h = natural death rate of humans 0.00004 [8]
μ_v = natural death rate of mosquitoes 0.05 [9]
r=education on drug use 0.5 [Assumed]
γ=loss of immunity rate 0.000017 [4, 10]
m=$\frac{N_V}{N_H}$ the number of female mosquitoes per human host [2, 23]

2.2 Assumptions of the Model

The following assumptions were made in order to formulate the equations of the model:

(a) The exposed humans recover and return to susceptible population if their immunity is able to combat the dormant parasites

(b) The exposed humans progress to become infectious if their immunity is unable to combat the dormant parasites

(c) The exposed humans are those who have dormant parasites in them i.e they cannot yet infect a susceptible mosquito

(d) All humans are born susceptible and there is no vertical transmission

(e) Some infectious human hosts who are given medication by their doctors and comply with drug (i.e they take the correct dosage and complete treatment) get treated fully and move to the recovered human host compartment.

(f) Some infectious human hosts who do not comply with drug get treated partially and move to non-drug compliant human compartment.

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

(g) Proportion of active parasites are still in the blood of non-drug compliant humans
(h) When a susceptible mosquito bites the non-drug compliant humans, it becomes infected
(j) Susceptible humans progress to become exposed.
(k) Recovered humans have some immunity that can be lost and again susceptible.

The population of susceptible humans is generated either by birth or immigration at a constant rate π_h. The interaction of humans and female mosquitoes is modelled by standard incidence [23], with the terms $\frac{abS_HI_V}{N_H}$, which denotes the rate at which susceptible humans S_H get infected by infected mosquitoes I_V. The population increases at the rate ν due to the recovery rate of the exposed humans (if the immune system of the exposed humans is able to combat the dormant plasmodium parasite because at the exposed stage, plasmodium parasites are still dormant in the liver). It increases again due to loss of immunity of recovered humans at the rates γ. The population also decreases when the susceptible humans die naturally at the rate μ_h. Putting all these together gives the following equation for the rate of change of the susceptible population:

$$\frac{dS_H}{dt} = \pi_h N_H - \frac{abS_HI_V}{N_H} + \nu E_H + \gamma R_H - \mu_h S_H$$

The population of exposed humans is generated as a result of progression of the susceptible humans who are infected with plasmodium falciparum by the infected mosquitoes but have not started displaying symptoms, i.e., they are infected but not yet infectious, with the terms $\frac{abS_HI_V}{N_H}$. It decreases as a result of recovery of the exposed humans and the progression of the exposed humans to become infectious(the dormant parasites undergo nuclear division and thousands of them move down to the blood stream, if the immune system is unable to combat the parasites at the exposed stage) at the rates ν and αab. It diminishes due to natural death at the rate μ_h. Thus,

$$\frac{dE_H}{dt} = \frac{abS_HI_V}{N_H} - \nu E_H - \frac{\alpha abs_HI_V}{N_H} - \mu_h E_H$$

The population of infectious humans is generated by the progression rate of the exposed humans at the rate αab. It diminishes due to drug efficacy τ, death due to malaria δ and natural death μ_h. Thus we have

$$\frac{dI_H}{dt} = \frac{\alpha abS_HI_V}{N_H} - \frac{\tau abS_HI_V}{N_H} - \delta I_H - \mu_h I_H$$

The population of non-drug compliant humans is generated by a fraction $(1-\theta)\tau$ of infectious humans who do not comply with drug. The population reduces due to non-drug compliance, education on drug use and natural death at the rates μ_N, $r\tau$ and μ_h so that

$$\frac{dI_{NH}}{dt} = \frac{(1-\theta)\tau abS_HI_V}{N_H} - \mu_N I_{NH} - r\tau I_{NH} - \mu_h I_{NH}$$

The population of recovered humans is generated by the fraction $\theta\tau$ of infectious humans who comply with drug. It reduces due to loss of immunity of the recovered humans and natural death at the rates γ and μ_h. It again increases due to education on drug use at the rate r τ. Thus,

$$\frac{dR_H}{dt} = \frac{\theta\tau abS_HI_V}{N_H} - \gamma R_H + r\tau I_{NH} - \mu_h R_H$$

In a similar way, the population of mosquito vector changes so that we have the following:

$$\frac{dS_V}{dt} = \pi_V N_V - \frac{apS_V(I_H + I_{NH})}{N_H} - \mu_V S_V$$

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

$$\frac{dI_V}{dt} = \frac{apS_V(I_H + I_{NH})}{N_H} - \mu_V I_V$$

Putting everything together, we have the following system of ordinary differential equations:

$$\begin{aligned}
\frac{dS_H}{dt} &= \pi_h N_H - \frac{abS_H I_V}{N_H} + \nu E_H + \gamma R_H - \mu_h S_H && (2.1)\\
\frac{dE_H}{dt} &= \frac{abS_H I_V}{N_H} - \nu E_H - \frac{\alpha abs_H I_V}{N_H} - \mu_h E_H && (2.2)\\
\frac{dI_H}{dt} &= \frac{\alpha abS_H I_V}{N_H} - \frac{\tau abS_H I_V}{N_H} - \delta I_H - \mu_h I_H && (2.3)\\
\frac{dI_{NH}}{dt} &= \frac{(1-\theta)\tau abS_H I_V}{N_H} - \mu_N I_{NH} - r\tau I_{NH} - \mu_h I_{NH} && (2.4)\\
\frac{dR_H}{dt} &= \frac{\theta\tau abS_H I_V}{N_H} - \gamma R_H + r\tau I_{NH} - \mu_h R_H && (2.5)\\
\frac{dS_V}{dt} &= \pi_V N_V - \frac{apS_V(I_H + I_{NH})}{N_H} - \mu_v S_v && (2.6)\\
\frac{dI_V}{dt} &= \frac{apS_V(I_H + I_{NH})}{N_H} - \mu_V I_V && (2.7)
\end{aligned}$$

The restriction on the initial population arises from the fact that the variables describe the dynamics of human and mosquito populations. Therefore, for the model to be biologically meaningful, all the initial conditions and parameters must be non-negative. Thus $S_H(0) \geq 0$, $E_H(0) \geq 0$, $I_H(0) \geq 0$, $I_{NH}(0) \geq 0$, $R_H(0) \geq 0$, $S_V(0) \geq 0$, $I_V(0) \geq 0$.

The total population sizes N_H and N_V are

$$\begin{aligned}
\frac{dN_H}{dt} &= (\pi_h - \mu_h)N_H - \delta I_H - \mu_N I_{NH} && (2.8)\\
\frac{dN_V}{dt} &= (\pi_v - \mu_v)N_V && (2.9)
\end{aligned}$$

which are derived by adding (2.1)-(2.5) for the human population and (2.6)-(2.7) for the mosquito vector population.

3 Transformation of the model

It is convenient to use fraction of population instead of population number. This is done by dividing each population class by the total population and hence, we have:

$s_h = \frac{S_H}{N_H}$; $i_h = \frac{I_H}{N_H}$; $e_h = \frac{E_H}{N_H}$, $i_{nh} = \frac{I_{NH}}{N_H}$, $r_h = \frac{R_H}{N_H}$; $s_v = \frac{S_V}{N_V}$; $i_v = \frac{I_V}{N_V}$; $m = \frac{N_V}{N_H}$.

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

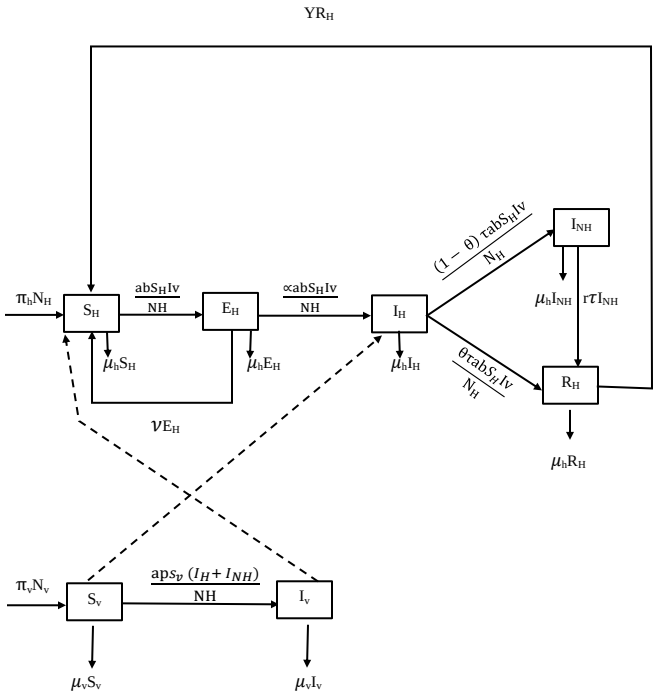

Diagram for Malaria Model Incorporating a New Class of Non-Drug Compliant Human Compartment

Differentiating the fraction with respect to time t gives the following:

$$\frac{ds_h}{dt} = \pi_h(1-s_h) - abms_hi_v + \nu e_h + \gamma r_h + \delta s_h i_h + \mu_N s_h i_{nh} \tag{3.1}$$

$$\frac{de_h}{dt} = abms_hi_v - (\nu+\pi_h)e_h - \alpha abms_hi_v + \delta e_h i_h + \mu_N e_h i_{nh} \tag{3.2}$$

$$\frac{di_h}{dt} = \alpha abms_hi_v - \tau abms_hi_v - (\delta+\pi_h)i_h + \delta i_h^2 + \mu_N i_h i_{nh} \tag{3.3}$$

$$\frac{di_{nh}}{dt} = (\tau-\theta\tau)abms_hi_v - (\mu_N + r\tau + \pi_h)i_{nh} + \delta i_h i_{nh} + \mu_N i_{nh}^2 \tag{3.4}$$

$$\frac{dr_h}{dt} = \theta\tau abms_hi_v - (\gamma+\pi_h)r_h + \delta i_h r_h + r\tau i_{nh} + \mu_N i_{nh} r_h \tag{3.5}$$

$$\frac{ds_v}{dt} = \pi_v(1-s_v) - aps_v(i_h+i_{nh}) \tag{3.6}$$

$$\frac{di_v}{dt} = aps_v(i_h+i_{nh}) - \pi_v i_v \tag{3.7}$$

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

From the relation $s_h+e_h+i_h+i_{nh}+r_h=1$ and $s_v+i_v=1$, it implies that $r_h=1-s_h-e_h-i_h-i_{nh}$ and $s_v=1-i_v$ which reduces to the following system of differential equations:

$$\frac{ds_h}{dt} = \pi_h(1-s_h) - abms_hi_v + \nu e_h + \gamma(1-s_h-e_h-i_h-i_{nh}) + \delta s_hi_h + \mu_N s_hi_{nh} \quad (3.8)$$

$$\frac{de_h}{dt} = abms_hi_v - (\nu+\pi_h)e_h - \alpha abms_hi_v + \delta e_hi_h + \mu_N e_hi_{nh} \quad (3.9)$$

$$\frac{di_h}{dt} = \alpha abms_hi_v - \tau abms_hi_v - (\delta+\pi_h)i_h + \delta i_h^2 + \mu_N i_hi_{nh} \quad (3.10)$$

$$\frac{di_{nh}}{dt} = (\tau-\theta\tau)abms_hi_v - (\mu_N+r\tau+\pi_h)i_{nh} + \delta i_hi_{nh} + \mu_N i_{nh}^2 \quad (3.11)$$

$$\frac{di_v}{dt} = api_h(1-i_v) + api_{nh}(1-i_v) - \pi_v i_v \quad (3.12)$$

3.1 Existence of Solutions

Here, we provide the following result which guarantees that the malaria model governed by the system (3.1)-(3.7) is epidemiologically well-posed in a feasible region Γ defined by

$\Gamma \in \Re_+^7$ and $\Gamma_h \cup \Gamma_v \subset \Re_+^5 * \Re_+^2$

Lemma 1: The solutions of the system are contained and bounded in the region, $\Gamma \in \Re^7$ and $\Gamma_c \cup \Gamma_t \subset \Re_+^5 * \Re_+^2$.

Proof: We show that the feasible solutions are uniformly bounded in proper subsets $\Gamma \in \Re_+^7$. Let $(s_h, e_h, i_h, i_{nh}, r_h, s_v, i_v) \in \Re^7$ be any solution of the system given by $N_h = s_h+e_h+i_h+i_{nh}+r_h$ and $N_v = s_v+i_v$ with non-negative initial conditions. In differential form, we write

$$\frac{dN_h}{dt} = \frac{ds_h}{dt} + \frac{de_h}{dt} + \frac{di_h}{dt} + \frac{di_{nh}}{dt} + \frac{dr_h}{dt}$$

$$\frac{dN_h}{dt} = \pi_h - (\pi_h - \delta i_h - \mu_N i_{nh})N_h - \delta i_h - \mu_N i_{nh}$$

since

$$s_h + e_h + i_h + i_{nh} + r_h = N_h$$

$$\frac{dN_h}{dt} = \pi_h - (\pi_h - \delta i_h - \mu_N i_{nh})N_h - \delta i_h - \mu_N i_{nh}$$

Hence we have

$$\frac{N_h}{dt} + (\pi_h - \delta i_h - \mu_N i_{nh})N_h = \pi_h - \delta i_h - \mu_N i_{nh}$$

Solving yields

$$N_h = 1 + Be^{-(\pi_h - \delta i_h - \mu_N i_{nh})t}$$

Applying the initial condition $N_h(0) = N_h^o$ leads to

$$N_h = 1 + (N_h^o - 1)e^{-(\pi_h - \delta i_h - \mu_N i_{nh})t}$$

Thus $N_h \to 1$ as $t \to \infty$

And

$$\frac{dN_v}{dt} = \pi_h - \pi_v N_v$$

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

$$\frac{dN_h}{dt} + \pi_v N_v = \pi_v$$

We solve to obtain

$$N_v = 1 + (N_v^o - 1)e^{-\pi_v t}$$

Thus $N_v \to 1$ as $t \to \infty$

Hence the feasible region for the model is given by

$\Gamma =$

$(s_h, e_h, i_h, i_{nh}, r_h, s_v, i_v) \in \Re_+^7; s_h, e_h, i_h, i_{nh}, r_h, s_v, i_v \geq 0, s_h + e_h + i_h + i_{nh} + r_h = 1; s_v + i_v = 1$ which is positively invariant set for the model system. Hence, the model is well-posed and biologically realistic and meaningful. Thus, all solutions of the human population only are confined in the feasible region Γ_h and all solutions of the mosquito vector population are confined in Γ_v

3.2 Basic Reproduction Number

The computation of the basic reproduction number R_o is needed in order to assess the global stability of disease-free equilibrium. This is obtained by expressing (3.8)-(3.12) as the difference between the rate of new infection in each infected compartment F and the rate of transfer between each infected compartment G. Hence, we have

$$\begin{bmatrix} \frac{de_h}{dt} \\ \frac{di_h}{dt} \\ \frac{i_{nh}}{dt} \\ \frac{i_v}{dt} \end{bmatrix} = F - G = \begin{bmatrix} abms_h i_v - \alpha abms_h i_v \\ \alpha abms_h i_v - \tau abms_h i_v \\ (\tau - \theta\tau) abms_h i_v \\ aps_v i_h - aps_v i_{nh} \end{bmatrix} - \begin{bmatrix} (\nu + \pi_h)e_h + \delta e_h i_h + \mu_N e_h i_{nh} \\ (\delta + \pi_h)i_h + \delta i_h^2 + \mu_N i_h i_{nh} \\ (\mu_N + r\tau + \pi_h)i_{nh} + \delta i_h i_{nh} + \mu_N i_{nh}^2 \\ \pi_v i_v \end{bmatrix}$$

The Jacobian matrices J_F and J_G of F and G are found about E_0.

$$S = J_F J_G^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{ap}{\pi_v} \\ 0 & 0 & 0 & \frac{ap}{\pi_v} \\ \frac{-abm\alpha + abm}{\nu + \pi_h} & \frac{-abm\tau + abm\tau}{\delta + \pi_h} & \frac{(-\tau\theta + \tau)abm}{r\tau + \mu_N + \pi_h} & 0 \end{bmatrix}$$

R_o is the maximum eigenvalue of S given as

$$R_o = \frac{a^2 bmp(r\tau\alpha - r\tau^2 - r\delta\theta - \tau\theta\pi_h + \tau\delta - \tau\mu_N + \alpha\mu_N + \alpha\pi_h)}{\pi_v(r\tau\delta + r\tau\pi_h + \delta\mu_N + \delta\pi_h + \mu_N\pi_h + \pi_h^2)}$$

$$R_o = \frac{a^2 bmp(r\tau\alpha - r\tau^2 - r\delta\theta - \tau\theta\pi_h + \tau\delta - \tau\mu_N + \alpha\mu_N + \alpha\pi_h)}{\pi_v A_T B_T}$$

where

$A_T = \delta + \pi_h$ and $B_T = \mu_N + r\tau + \pi_h$

4 Results and Discussions

4.1 Global Stability of the disease-free equilibrium

The disease-free equilibrium solution is obtained by setting the right-hand side of (3.8)-(3.12) to zero to obtain $E_o = (1, 0, 0, 0, 0)$. Hence, we provide the dynamical behaviour of the model (3.8)-(3.12) as its solution trajectories approach the disease-free equilibrium solution in what follows:

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

Theorem 1: The disease-free equilibrium E_o of (3.8)-(3.12) is globally asymptotically stable in Γ if $R_o \leq 1$ and unstable if $R_o > 1$.

Proof: Consider the Lyapunov function $L = apr\delta\theta e_h + (apr\tau + ap\mu_N + ap\pi_h)i_h + (apr\alpha + ap\pi_h + ap\delta)i_{nh} + A_T B_T i_v$. Its time derivative is

$$\begin{aligned}
L' &= apr\delta\theta\frac{de_h}{dt} + (apr\tau + ap\mu_N + ap\pi_h)\frac{di_h}{dt} + (apr\alpha + ap\pi_h + ap\delta)\frac{di_{nh}}{dt} + A_T B_T\frac{di_v}{dt} \\
&= apr\delta\theta(abms_h i_v - C_T e_h - \alpha abms_h i_v + \delta e_h i_h + \mu_N e_h i_{nh}) + \\
&\quad (apr\tau + ap\mu_N + ap\pi_h)(\alpha abms_h i_v - \tau abms_h i_v - A_T i_h + \delta i_h^2 + \mu_N i_h i_{nh}) + \\
&\quad (apr\alpha + ap\pi_h + ap\delta)(\tau abms_h i_v - \theta\tau abms_h i_v - B_T i_{nh} + \delta i_h i_{nh} + \mu_N i_{nh}^2) + \\
&\quad A_T B_T[api_h(1 - i_v) + api_{nh}(1 - i_v) - \pi_v i_v] \\
&= a^2 bmp(r\tau\alpha - r\tau^2 - r\delta\theta - \tau\theta\pi_h + \tau\delta - \tau\mu_N + \alpha\mu_N + \alpha\pi_h)s_h i_v - \\
&\quad A_T B_T\pi_v i_v - Dape_h - Eapi_h - Fapi_{nh} - Ga^2 bmps_h i_v \\
&= A_T B_T\pi_v i_v\left(\frac{a^2 bmp(r\tau\alpha - r\tau^2 - r\delta\theta - \tau\theta\pi_h + \tau\delta - \tau\mu_N + \alpha\mu_N + \alpha\pi_h)s_h}{A_T B_T\pi_v} - 1\right) - \\
&\quad Dape_h - Eapi_h - Fapi_{nh} - Ga^2 bmps_h i_v \\
&= A_T B_T\pi_v i_v(R_o s_h - 1) - Dape_h - Eapi_h - Fapi_{nh} - Ga^2 bmps_h i_v \\
&\quad \leq A_T B_T\pi_v i_v(R_0 s_h - 1) \leq 0 \quad \text{if} \quad R_0 \leq 1
\end{aligned}$$

where

$A_T = \delta + \pi_h$

$B_T = \mu_N + r\tau + \pi_h$

$C_T = \nu + \pi_h$

$D = r\delta\theta C_T - \delta^2 i_h r\theta - \mu_N i_{nh} r\delta\theta$

$E = A_T r\tau + A_T\mu_N + A_T B_T i_v + A_T\pi_h - \delta i_h r\tau - \mu_N i_{nh} r\tau - \delta i_h\mu_N - \mu_N i_{nh}^2 - \delta i_h\pi_h - \mu_N i_{nh}\pi_h - \delta i_{nh} r\alpha - \delta i_{nh}\pi_h - \delta^2 i_{nh} - A_T B_T$

$F = B_T r\alpha + B_T\pi_h + B_T\delta + A_T B_T i_v - A_T B_T - i_{nh}\mu_N\delta - i_{nh}\mu_N\pi_h - \mu_N i_{nh} r\alpha$

$G = \alpha r\delta\theta + \tau\pi_h + \theta\tau r\alpha - \theta\tau\delta - \tau r\alpha - \tau\pi_h$

Therefore, $L' \leq 0$ for $R_o \leq 1$. One sees further that $(s_h, e_h, i_h, i_{nh}, i_v) \to (1, 0, 0, 0, 0)$ as $t \to \infty$. Consequently, the largest compact invariant set in $\{(s_h, e_h, i_h, i_{nh}, i_v) \in \Gamma : L' = 0\}$ is the E_0 and by Lyapunov-Lasalle's principle [14, 12], the disease-free equilibrium point is globally asymptotically stable in Γ if $R_o \leq 1$ and this completes the proof of Theorem 1. The epidemiological implication of the result implies that the disease can be eradicated with population that starts with either large or small number of infectious humans whenever $R_o < 1$.

4.2 Local Stability of Endemic Equilibrium

We shall first show the interval where the endemic equilibrium exists using the idea of Tumwiine et al.[23]. Hence, for the existence and uniqueness of endemic equilibrium $E_1 = (s_h^*, e_h^*, i_h^*, i_{nh}^*, i_v^*)$, its coordinates should satisfy the conditions $s_h^* > 0, e_h^* > 0, i_h^* > 0, i_{nh}^* > 0, i_v^* > 0$. Adding (3.8)-(3.12), we have

$\pi_h(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) + \gamma(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) - \delta i_h^*(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) - \mu_N i_{nh}^*(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) + api_h^*(1 - i_v^*) + api_{nh}^*(1 - i_v^*) - \pi_v i_v^* + r\tau i_{nh}^* - \theta\tau abms_h^* i_v^* = 0$

From (3.12), $api_h^*(1 - i_v^*) + api_{nh}^*(1 - i_v^*) - \pi_v i_v^* = 0$

This yields

$(\pi_h + \gamma - \delta i_h^* - \mu_N i_{nh}^*)(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) = \theta\tau abms_h^* i_v^* - r\tau i_{nh}^*$.

Since $(1 - s_h^* - e_h^* - i_h^* - i_{nh}^*) > 0$ and $\theta\tau abms_h^* i_v^* - r\tau i_{nh}^* > 0$, then

$$\pi_h + \gamma - \delta i_h^* - \mu_N i_{nh}^* > 0 \tag{4.1}$$

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

Further simplification gives

$\pi_h + \gamma > \delta i_h^* + \mu_N i_{nh}^*$

since death due to non-drug compliance μ_N implies death due to malaria δ, then

$\mu_N = \delta$

Therefore, $\pi_h + \gamma > \delta i_h^* + \delta i_{nh}^*$

$\delta(i_h^* + i_{nh}^*) < (\lambda_h + \gamma)$

This gives

$(i_h^* + i_{nh}^*) < \dfrac{\lambda_h + \gamma}{\delta}$.

Therefore, an endemic equilibrium point exists, where $(i_h^* + i_{nh}^*)$ lie in the interval $\left(0, \min\left\{1, \frac{\lambda_h+\gamma}{\delta}\right\}\right)$. If $\delta < \lambda_h + \gamma$, the interval becomes large and this means that malaria persists in the population.

We next analyze the stability of endemic equilibrium E_1 using the Jacobian matrix computed for (3.8)-(3.12) given by

$$J_{E_1} = \begin{bmatrix} J_{11} & \nu - \gamma & -\gamma + \delta s_h^* & -\gamma + \mu_N s_h^* & -abms_h^* \\ abmi_v^* - \alpha abmi_v^* & J_{22} & \delta e_h^* & \mu_N e_h^* & abms_h^* - \tau abms_h^* \\ \alpha abmi_v^* - \tau abmi_v^* & 0 & J_{33} & \mu_N i_h^* & \alpha abms_h^* - \tau abms_h^* \\ \tau abmi_v^* - \theta\tau abmi_v^* & 0 & \delta i_{nh}^* & J_{44} & \tau abms_h^* - \theta\tau abms_h^* \\ 0 & 0 & ap(1 - i_v^*) & ap(1 - i_v^*) & -\pi_v^* \end{bmatrix} \tag{4.2}$$

where

$J_{11} = -\pi_h - abmi_v^* - \gamma + \delta i_h^* + \mu_N i_{nh}^*$

$J_{22} = -\nu - \pi_h + \delta i_h^* + \mu_N i_{nh}^*$

$J_{33} = -\delta - \pi_h + 2\delta i_h^* + \mu_N i_{nh}^*$

$J_{44} = -\mu_N - r\tau - \pi_h + \delta i_h^* + 2\mu_N i_{nh}^*$

Using Sarrus diagram, i.e.,

$a_1b_2c_3d_4e_5 + a_2b_3c_4d_5e_1 + a_3b_4c_5d_1e_2 + a_4b_5c_1d_2e_3 + a_5b_1c_2d_3e_4 - a_1b_5c_4d_3e_2 - a_2b_1c_5d_4e_3 - a_3b_2c_1d_5e_4 - a_4b_3c_2d_1e_5 - a_5b_4c_3d_2e_1$,

the characteristic equation of the Jacobian matrix (4.2) at the endemic equilibrium point $E_1 = (s_h^*, e_h^*, i_h^*, i_{nh}^*, i_v^*)$ is a fifth degree polynomial given by

$$\lambda^5 + a_1\lambda^4 + a_2\lambda^3 + a_3\lambda^2 + a_4\lambda + a_5 \quad = \quad 0 \tag{4.3}$$

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

where

$$
\begin{aligned}
a_0 &= 1\\
a_1 &= (abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*) + (api_h^* + api_{nh}^* + \pi_v) + (\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*) +\\
&\quad (\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*)\\
a_2 &= (\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*)(\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*)\\
&\quad +(api_h^* + api_{nh}^* + \pi_v)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* + \mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad (abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* + \mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad (abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*)(api_h^* + api_{nh}^* + \pi_v) + (abmi_v^* + \pi_h - \gamma - \delta i_h^* - \mu_N i_{nh}^*)\\
&\quad (\nu + \pi_h - \delta i_h^* - \mu_N i_{nh}^*)\\
a_3 &= [(api_h^* + api_{nh}^* + \pi_v)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*)(\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad (abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*)\\
&\quad (\mu_N + r\tau + \pi_h - \delta i_{nh}^* - \mu_N i_{nh}^*) + (abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*)(api_h^* + api_{nh}^* + \pi_v)\\
&\quad (\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* + \mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad (abmi_v^* + \pi_h - \gamma - \delta i_h^* - \mu_N i_{nh}^*)(\nu + \pi_h - \delta i_h^* - \mu_N i_{nh}^*)\\
&\quad (\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* + \mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad (api_h^* + api_{nh}^* + \pi_v)(abmi_v^* + \pi_h - \gamma - \delta i_h^* - \mu_N i_{nh}^*)(\nu + \pi_h - \delta i_h^* - \mu_N i_{nh}^*)]\\
a_4 &= [(abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - 2\mu_N i_{nh}^*)(api_h^* + api_{nh}^* + \pi_v)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*)\\
&\quad (\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) + (api_h^* + api_{nh}^* + \pi_v)\\
&\quad (\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* + \mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*)]\\
a_5 &= (abmi_v^* + \pi_h - \gamma - \delta i_h^* - \mu_N i_{nh}^*)(\nu + \pi_h - \delta i_h^* - \mu_N i_{nh}^*)\\
&\quad (api_h^* + api_{nh}^* + \pi_v)(\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^*)(\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad abm(\nu - \gamma)ap(1 - i_v^*)(\alpha - a)s_h^*(\mu_N + r\tau + \pi_h + \delta i_{nh}^* - 2\mu_N i_{nh}^*) +\\
&\quad a^2b^2m^2 i_v^* s_h^*(\tau - \alpha)ap(1 - i_v^*)(\nu + \pi_h - \delta i_h^* - \mu_N i_{nh}^*)(\delta s_h^* - \gamma) = 0
\end{aligned}
$$

Clearly, $a_0 > 0$. Since $\pi_h+\gamma-\delta i_h^*-\mu_N i_{nh}^* > 0$ from (4.1), then $abmi_v^*+\gamma+\nu+2\pi_h-2\delta i_h^*-\mu_N i_{nh}^* > 0$, $\delta+\pi_h-2\delta i_h^*-\mu_N i_{nh}^* > 0$ and $\mu_N+r\tau+\pi_h-\delta i_{nh}^*-2\mu_N i_{nh}^* > 0$. Clearly, $api_h^*+api_{nh}^*+\pi_v > 0$. It then follows that $a_1 > 0$, $a_2 > 0$, $a_3 > 0$, $a_4 > 0$ and $a_5 > 0$ for $abmi_v^* + \gamma + \nu + 2\pi_h - 2\delta i_h^* - \mu_N i_{nh}^* > 0$, $\delta + \pi_h - 2\delta i_h^* - \mu_N i_{nh}^* > 0$, $\mu_N + r\tau + \pi_h - \delta i_{nh}^* - 2\mu_N i_{nh}^* > 0$ and $api_h^* + api_{nh}^* + \pi_v > 0$. Therefore, all the coefficients $a_i s$ are positive. The necessary and sufficient conditions for the local stability of the endemic equilibrium E_1 are that the Hurwitz determinants, H_i, are all positive for the Routh-Hurwitz criteria [18]. Hence, since $a_1 > 0$, $a_2 > 0$, $a_3 > 0$, $a_4 > 0$ and $a_5 > 0$, then

$H_1 > 0$,
$H_2 > a_1a_2 - a_3 > 0$,
$H_3 = a_1a_2a_3 + a_1a_5 - a_1^2a_4 - a_3^2 > 0$,
$H_4 = (a_3a_4 - a_2a_5)(a_1a_2 - a_3) - (a_1a_4 - a_5)^2 > 0$,
$H_5 = a_5H_4 > 0$

Therefore by Routh-Hurwitz theorem [15, 18], all the eigenvalues of the polynomial $P(\lambda)$ have negative real parts and the endemic equilibrium is locally asymptotically stable.

The theorem below summarizes the above result:

Theorem: The endemic equilibrium is locally asymptotically stable if all the eigenvalues of the polynomial $P(\lambda)$ have negative real part.

IJMAO

International Journal of Mathematical Analysis and Optimization: Theory and Applications
Vol. 2019, No. 2, pp. 558 - 570

5 Discussion of Results and Conclusion

In this work, a mathematical model is formulated and analysed to study the transmission and spread of malaria parasite in a population. The model incorporates a class of non-drug compliant human compartment into the population. A 7-dimensional system of nonlinear ordinary differential equations is modelled. It is shown that there exist a domain Γ where the model is well-posed and biologically meaningful. The disease-free equilibrium points of the model are obtained and analysed for stability. The condition for disease spread which is the basic reproduction number, R_0, is calculated respectively. It is shown that when $R_0 < 1$, malaria is cleared from the population. Whereas, if $R_0 > 1$, the disease persists in the population. Thus, a new class of non-drug compliant humans can contribute to the spread of malaria as susceptible mosquitoes get infected when they bite this group thereby spreading malaria in the population. Also, public health can educate people on the effect of the incorporated non-drug compliant human compartment on transmission dynamics of malaria model by using this article as a study guide for seminars, workshop or training programs.

References

[1] Alles, H.K., Mendis, K.N., & Carter, R. Malaria mortality rates in South Asia and in Africa:implications for malaria control *Parasitology Today*, 14, 369-375, (1998).

[2] Aneke, S.J. Mathematical modeling of drug resistant malaria parasites and vector populations.*Mathematical Methods in the Applied Sciences*, 90, 385-396, (2012).

[3] Antino, B., Corbett, Y., Catelli, F. & Taramelli, D. Pathogenesis of malaria in tissues and blood.*Mediterranean Journal of Hematology and Infectious Diseases*, 2035-3006, (2012).

[4] Aron, J.L. Mathematical modeling of immunity to malaria. *Mathematical Biosciences*, 90, 385-396, (1982).

[5] Bakary, T., Sangare, B. & Traore, S. Mathematical modeling of malaria transmission with structured vector population and seasonality. *Journal of Applied Mathematics*, 15, (2017).

[6] Blayneh, K., Cao, Y. & Kwon, H. Optimal control of vector-borne diseases. Treatment and prevention. *Discrete Continuous Dyn Syst Ser B*, 11, 587-611, (2009).

[7] Chitnis, N., Cushing, J.M & Hyman, J.M. Bifurcation analysis of a mathematical model for malaria transmission. *SIAM Journal of Applied Mathematics*, 67, 24-45, (2018).

[8] Coutinho, F.A.B., Burattini, M.N., Lopez, L.F. & Massad, E. An approximate threshold condition for non-autonomous system:an application to a vector-borne infection. *Mathematics and Computer in Simulation*, 70, 149-158, (2005).

[9] Gemperli, A., Vounatsou P., Sogoba, N. & Smith, T. Malaria mapping using transmission models: application to survey data. *American Journal of Epidemiology*, 163, 289-297, (2006).

[10] Ishikawa, H., Ishii, A., Nagai, N., Ohmae, H., Mazakazu, H., Shuguri, S. & Leafasia, J. A mathematical model for the transmission of plasmodium vivax malaria. *Parasitology International*, 52, 81-93, (2013).

[11] Jongwutiwes, S., Putaporntip, C., Iwasaki, T., Sata T. & Kanbara, H. Naturally acquired plasmodium knowlesi in malaria in human, Thailand. *Emerging Infectious Diseases*, 10, 2211-2232, (2010).

[12] Khalil, H. Nonlinear systems. *Prentice Hall*, (2002).

[13] Laxminarayan, R. Act now or later? Economics of malaria resistance. *The American Journal of Tropical Medicine and Hyiegene*, 71, 187-195 (2004).

[14] Lasalle, J.P. The stability of dynamical systems. *Philadelphia, PA: SIAM*, (1976).

[15] Lancaster, P. Theory of matrices. *Academic Press, New York*, (1969).

[16] Lieshonta, M.V., Kovats, R.S., Livermore, M.T.J & Martens, P. Climate change and malaria: analysis of the SRES climate and socio-economic scenarios. *Global Environmental Change*, 14, 87-99 (2004).

[17] Murray, C.J.L, Rosenfeld, L.C., Lim, S.S., Andrews, K.G., Foreman, K.J., Haring, D., Fullman, N., Naghari, M., Lozano, R. & Lopez, A.D. Global malaria mortality between 1980 and 2010: a systematic analysis. *The Lancet*, 379, 413-431 (2012).

[18] Murray, J.D. Mathematical Biology I, An introduction. *Springer-Verlag, Berlin*, (2002).

[19] Macdonald, G. The epidemiology and control of malaria. *Oxford: Oxford University Press*, (1957).

[20] Ousmane, K., Traore, B. & Sangare, B. Mathematical modeling of malaria transmission global dynamics: taking into account the immatured stages of the vectors. *Advances in Difference Equations*, 22, (2018).

[21] Tumwiine, J., Mugisha, J.Y.T & Luboobi, L.S. On oscillatory pattern of malaria dynamics in a population with temporary immunity. *Computational and Mathematical Mathematical Methods in Medicine*, 8, 191-203, (2007).

[22] Tumwiine, J., Luboobi, L.S. & Mugisha, J.Y.T. Modeling the effect of treatment and mosquito control on malaria transmission. *International Journal of Management and Systems*, 21, 107-124, (2005).

[23] Tumwiine, J., Mugisha, J.Y.T & Luboobi, L.S. A mathematical model for the dynamics of malaria in a human host and mosquito vector with temporary immunity. *Applied Mathematics and Computation* , 189, 1953-1965, (2007).

[24] Wedajo, A.J., Bole, B.K, Koya, P.R. Analysis of SIR mathematical model for malaria disease with the inclusion of infected immigrants. *IOSR Journal of Mathematics*, 14, 10-21, (2018).

[25] World Health Organization. World malaria report. *WHO Library Cataloguing-in-publication data*, (2013).

[26] World Health Organization. Malaria control in complex emergencies, an inter-agency field handbook. *WHO Library Cataloguing-in-publication data*, (2005).