MATHEMATICAL MODEL OF MALARIA TRANSMISSION WITH ANTI-MALARIAL HERBAL THERAPY AS CONTROL

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ABSTRACT: *Conventional anti–malarial drugs (chloroquine, Artesunate, Quinine, Amodiaquine etc) are used by most malaria-endemic countries as first-line treatment for uncomplicated malaria. However, resistance by plasmodium parasite against these conventional anti–malarial drugs has necessitated the need for herbal medicine as alternative. So in this study, we formulate a mathematical model of malaria transmission in two interacting population of human (host) and mosquito (vector) incorporating anti-malarial herbal therapy as first line treatment for uncomplicated malaria infection. The region where the model is epidemiological feasible and mathematically well–posed is established and the basic reproduction number R_0 is derived using next generation matrix approach. The numerical experiment carried out to access the impact of the control measure on malaria transmission revealed a reduction in the number of complicated infectious human population. Hence this research work suggests a massive campaign on use of anti-malarial herbal therapy as first- line treatment for malaria infection cases.*

KEYWORDS: Herbal Therapy, Malaria, Uncomplicated, Anti-Malarial

INTRODUCTION

Malaria is one of the most complex parasite vector–borne infectious diseases in the world and it is caused by the protozoan parasite of the genus *Plasmodium* which is transmitted to humans through bites of infectious female anopheles mosquitoes. (World Health Organization (WHO), 2021; Aguilar & Gutierrez, 2020). In rare cases, people may be infected via contaminated blood, or a fetus may become infected by its mother during pregnancy, during delivery or after delivery. (Oluwafemi & Azuaba, 2022)   This life–threatening disease is curable and it is usually categorized based on the clinical symptoms as asymptomatic, uncomplicated (mild), and complicated (severe) malaria. Asymptomatic malaria is defined as a case where an individual harbor the parasite capable of transmitting the disease but without exhibiting clinical symptoms as a result of naturally acquired immunity which develops slowly with age. Individuals with uncomplicated malaria are usually presented with fever and one or more of the following symptoms: chills and sweats, headache, vomiting, watery diarrhea and anemia but no clinical or laboratory evidence of vital organ dysfunction. In contrast, severe malaria is defined by at least one of the several clinical manifestations such as: coma (caused by cerebral malaria), convulsion, malarial anemia, hypoglycemia, metabolic acidosis (associated with respiratory distress), high fever and/or spontaneous bleeding (WHO, 2020; Bakary, Boureima, & Sado, 2018)

The World Health Organization (2021) reported that in 2020, an estimated 241 million cases of malaria occurred globally, most of the cases were in the WHO Africa region (96%) with Nigeria having the highest number of malaria cases globally (27% of the global cases in 2020), followed by the WHO South–East Asia Region (2%), then the WHO Eastern Mediterranean region (1.2%) and others (0.8%). It further estimated that 602,000 deaths from malaria occurred worldwide and Nigeria accounted for the highest malaria related deaths (23% of the global malaria deaths in 2019). Malaria has the highest burden of disease in Nigeria with an estimated 30,000 children dying of malaria each year. It accounts for over 25% of infant mortality (children under aged one), 30% of childhood mortality (children under age five), and 11% of maternal mortality. At least 50% of the population has at least one episode of malaria annually, while children aged less than 5 years have 2 to 4 attacks annually. Malaria is mostly severe in pregnancy and children less than 5 years of age due to their relatively low levels of immunity (Muhammad, Abdulkareem & Chowdhury 2017). No doubt, malaria remains a big public health problem in Nigeria; thus the need to have a mathematical study of malaria transmission dynamics in Nigeria with a view to providing workable preventive and control measures. Mathematical modeling has become an important tool in understanding the transmission dynamics of infectious diseases, considering appropriate control measure regarding intervention strategies for preventing and controlling the disease and planning for the future. Models can estimate the impact of a control measure and provide useful guidelines to public health officials and disease control centers for further efforts required for disease elimination. It can also predict whether disease will spread through the population or die out (Ndamuzi & Gahungu, 2021; Olaniyi & Obabiyi, 2013; Isere., Osemwenkhae. & Okuonghae, 2014)

Mandal, Sinha and Sarkar (2011) reported that Ronald Ross in 1911 introduced the first deterministic differential equations model for the control of malaria by dividing the human population into susceptible S_h and infected I_h compartments, with the infected class returning to susceptible class again leading to the SIS (Susceptible-Infected-Susceptible)

structure. The mosquito population also has only two compartments, S_m and I_m denoting the susceptible and infected mosquito classes respectively. Mosquitoes do not recover from infection due to their short life span and thereby follow the SI (Susceptible-Infected) structure. Mandal et al, (2011) further stated that the simple Ross model did not consider this latency period of the parasite in mosquitoes and their survival during that period. This resulted in the model predicting a rapid progress of the epidemic in human, and a higher equilibrium prevalence of infectious mosquitoes. Therefore, Macdonald in 1957 modified the Ross' model by considering the latency period of the parasites in mosquitoes and their survival during that period. Further extension was described by Anderson and May in 1991 where the latency of infection in humans was introduced by adding the exposed class in humans.

Over the years, several mathematical models of malaria transmission dynamics have been developed incorporating different factors to make them more biologically realistic in explaining disease prevalence and predictions. For example, a number of epidemiological studies considered the inclusion of the recovered class in human which incorporate a time dependent immunity developed on recovery from infection. (Bakare & Nwozo, 2015; Otieno, Koske & Mutiso, 2016). Other researchers have also incorporated different factors such as the impact of Artemisinin-based Combination Therapy (ACT) and other interventions on malaria prevalence (Okell, Drakeley, Bousema, Whitty, & Ghani, 2008; Griffin, Hollingsworth, Okell, Churcher, & White, 2010), impact of domestic animals or genetically-modified mosquitoes on the transmission of malaria (Diaz, Ramirez, Olarte, & Clavijo, 2011), effect of weather and climate change on transmission (Parham & Michael 2010), acquisition of immunity to malaria (Filipe, Riley, Darkeley, Sutherland & Ghani, 2007; Gurarie, Karl, Zimmerman, King & St. Pierre, 2012). Asymptomatic malaria models have also been developed and studied (Mandal, Sinha & Sarkar, 2013; Bakary, Boureima & Sado, 2018; Anguilar & Gutierrez, 2020). None of these models incorporates the progression of mild (uncomplicated) malaria cases to severe (complicated) malaria.

Studies have shown that complicated malaria is the principal cause of malaria related deaths (Laishram et al., 2012). Therefore, there is need to incorporate and study the progression of infectious host population from mild to complicated cases in malaria model, while taking into consideration the use of anti-malaria herbal therapy which confer protection against severe malaria. This could help better understand the transmission dynamics of malaria and also strengthen control strategies in reducing malaria related mortality. The anti-malaria herbal therapy has been applauded in medical literature to be very effective in the control of malaria in Nigeria. (Adebayo & Krettli, 2010; Oladeji, Oluyori, Bankole & Afolabi, 2020). Studies have also shown that some genetic traits (such as heterozygote HbAS , blood group O antigen rhesus type) confer protection against complicated malaria.(de Mendonca, Goncalves & Barral-Netto, 2012; Hedrick, 2011). So in this work, we propose a mathematical model for the control of malaria incorporating the progression of infectious host population from mild to severe malaria compartment while taking into consideration the use of anti-malaria herbal therapy as first-line treatment for mild malaria infection.

BASIC MODEL ASSUMPTIONS

We formulate our model taking into considerations the following basic assumptions:

(a)   All parameters in the model are non-negative

(b)   The total human population varies with time

(c)   The uncomplicated compartment consists of infectious persons with mild cases and asymptomatic carriers.

MODEL FORMULATION

The model comprises of two interacting population of human (host) and mosquito (vector) at time t denoted by $N_h(t)$ and $N_m(t)$ respectively. The human population is further divided into five compartments at any time t; Susceptible $S_h(t)$, Exposed $E_h(t)$, Uncomplicated (Mild) $M_h(t)$, Complicated $C_h(t)$ and recovered $R_h(t)$ human compartments. On the other hand, the mosquito population is divided into three compartments at any time t; Susceptible $S_m(t)$, Exposed $E_m(t)$ and Infectious $I_m(t)$ mosquito compartments. Hence we have that:

$$N_h(t) = S_h(t) + E_h(t) + M_h(t) + C_h(t) + R_h(t)$$

and

$$N_m(t) = S_m(t) + E_m(t) + I_m(t)$$

The compartmental model which shows the mode of transmission of malaria between the two interacting populations is shown in the figure below:
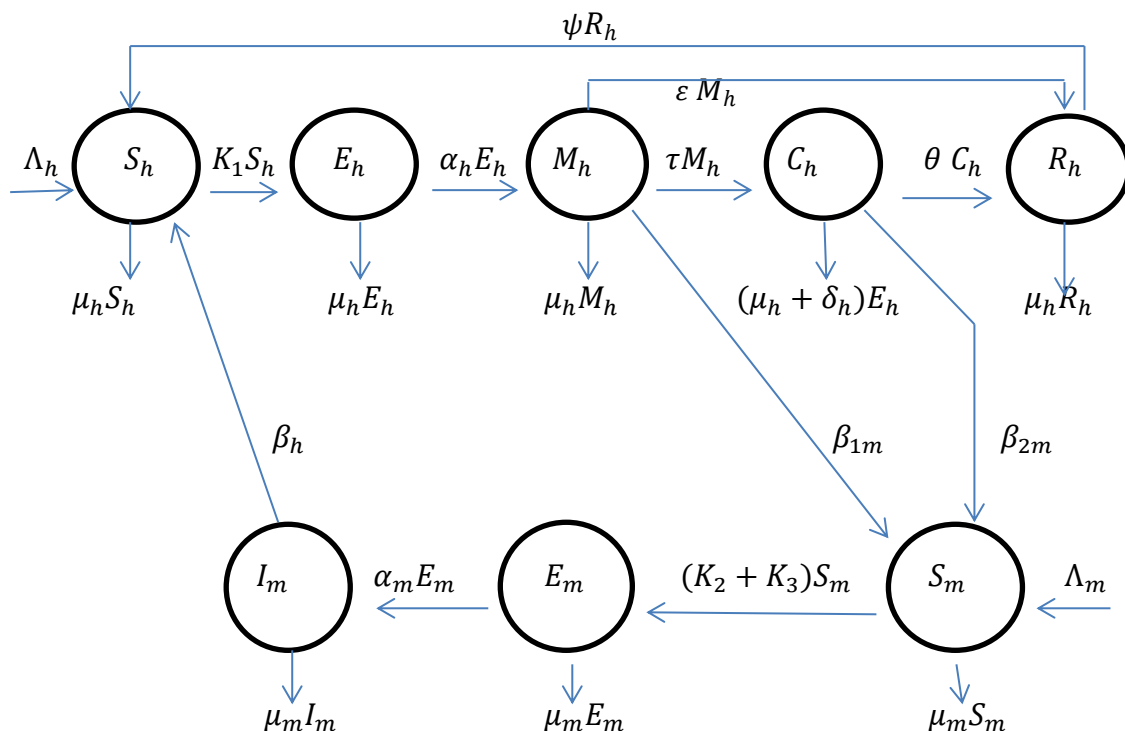

$Figure$ 1: **Compartmental model which shows the mode of transmission of malaria**

where $\varepsilon = \emptyset + g, \quad K_1 = \dfrac{b\beta_h I_m}{1+eI_m}, \quad K_2 = \dfrac{b\beta_{1m}M_h}{1+eM_h} \quad$ and $\quad K_3 = \dfrac{b\beta_{2m}C_h}{1+eC_h}$

The state variable and parameters used for the transmission model are described in the following tables:

Table 1: DESCRIPTION OF STATE VARIABLES OF THE MODEL

$S_h(t)$	Number of humans susceptible to malaria infection at time t
$E_h(t)$	Number of humans exposed to malaria infection at time t
$M_h(t)$	Number of infectious humans with uncomplicated/asymptomatic malaria infection at time t
$C_h(t)$	Number infectious humans with complicated cases of malaria infection at time t
$R_h(t)$	Number of recovered humans at time t
$S_m(t)$	Number of susceptible mosquitoes at time t
$E_m(t)$	Number of exposed mosquitoes at time t
$I_m(t)$	Number of infectious mosquitoes at time t

Table 2: DESCRIPTION OF MODEL PARAMETERS

Λ_h	Recruitment rate of susceptible humans
Λ_m	Recruitment rate of susceptible mosquitoes
μ_h	Per capita natural mortality rate of humans
μ_m	Per capita natural mortality rate of mosquitoes
δ_h	Per capita disease – induced mortality rate of humans
b	Per capita biting rate of mosquitoes
β_h	Probability that a bite by an infectious mosquito on a susceptible human results in transmission of disease to the susceptible human
β_{1m}	Probability that a bite by a susceptible mosquito results in transmission of disease from a mild/ asymptomatic infectious human to the susceptible mosquito
β_{1m}	Probability that a bite by a susceptible mosquito results in transmission of disease from a complicated infectious human to the susceptible mosquito
α_h	Per capita latent period in human
α_m	Per capita latent period in mosquito
ψ	Per capita loss of immunity by recovered humans
e	Rate constant of human behavior change
ε	Per capita treatment rate (recovery rate $\emptyset$ due natural immunity and treatment rate g due to the use of anti-malarial herbal drugs)
τ	Per capita rate of progression to infectious complicated human compartment
θ	Per capita progression rate to recovered compartment

From the model compartmental model in figure 1, we obtain an eight – dimensional system of ordinary differential equations which describe the progress of the disease as:

$$\frac{dS_h}{dt} = \Lambda_h + \psi R_h - \left(\frac{b\beta_h I_m}{1 + eI_m} + \mu_h\right)S_h$$

$$\frac{dE_h}{dt} = \left(\frac{b\beta_h I_m}{1 + eI_m}\right)S_h - (\alpha_h + \mu_h)E_h$$

$$\frac{dM_h}{dt} = \alpha_h E_h - (\varepsilon + \tau + \mu_h)M_h$$

$$\frac{dC_h}{dt} = \tau M_h - (\theta + \mu_h + \delta_h)C_h$$

$$\frac{dR_h}{dt} = \varepsilon M_h + \theta C_h - (\psi + \mu_h)R_h$$

$$\frac{dS_m}{dt} = \Lambda_m - b\left(\frac{\beta_{1m}M_h}{1 + eM_h} + \frac{\beta_{2m}C_h}{1 + eC_h}\right)S_m - \mu_m S_m$$

$$\frac{dE_m}{dt} = b\left(\frac{\beta_{1m}M_h}{1 + eM_h} + \frac{\beta_{2m}C_h}{1 + eC_h}\right)S_m - (\alpha_m + \mu_m)E_m$$

$$\frac{dI_m}{dt} = \alpha_m E_m - \mu_m I_m$$

(1)

with the initial conditions:

$S_h(0) = S_{0h},$ $\qquad E_h(0) = E_{0h},$ $\qquad M_h(0) = M_{0h},$ $\qquad C_h(0) = C_{0h}$

$R_h(0) = R_{0h}$ $\qquad S_m(0) = S_{0m},$ $\qquad E_m(0) = E_{0m},$ $\qquad I_m(0) = I_{0m}$

It can be seen in figure 1 that the susceptible humans are recruited into susceptible compartment by birth/immigration at per capital recruitment rate Λ_h and from recovered class following loss of partial immunity at per capital rate ψ. This compartment (population of susceptible human) is reduced by natural death at per capita death rate μ_h and by progression to exposed human class after effective contacts with infectious mosquitoes at infective rate $\frac{b\beta_h I_m}{1 + eI_m}$, where b, β_h and e represent the biting rate of mosquitoes, the probability that a bite by an infectious mosquito results in transmission of disease to a susceptible human and the rate constant of human behavior change.

The exposed human compartment is reduced by natural death at per capital rate μ_h and by progression to uncomplicated class at per capital progression rate α_h. The population of infectious human with uncomplicated cases is decreased by per capita natural death rate μ_h, per capita rate τ of progression to infectious complicated human compartment, recovery rate per capital g due to anti-malarial herbal drugs and spontaneous recovery rate per capital ϕ due to immunity

The complicated human compartment is reduced by per capita disease – induced death rate δ_h, per capita natural death rate μ_h and per capita recovery rate θ due to treatment.

Similarly, mosquitoes are recruited into susceptible mosquito compartment at per capital rate Λ_m. Susceptible mosquito becomes infected after taking in blood meal from malaria infectious humans at infective rate $b\left(\frac{\beta_{1m}M_h}{1 + eM_h} + \frac{\beta_{2m}C_h}{1 + eC_h}\right)$, where β_{1m} and β_{2m} represent the

probability that a bite results in transmission of disease from an uncomplicated infectious human to a susceptible mosquito and the probability that a bite results in transmission of disease from a complicated infectious human to a susceptible mosquito respectively. Mosquito population decline due to natural death at per capita death rate μ_m.

INVARIANT REGION;

Lemma 1: The model system (1) has solutions which are contained in the feasible region

$D = D_h \times D_m$

Proof: Let $D = \{S_h, E_h, M_h, C_h, R_h, S_m, E_m, I_m\} \in \mathbb{R}_+^8$ be any solution of the system with non-negative initial conditions. From the differential equations (1), we have:

$$\frac{dN_h(t)}{dt} = \Lambda_h - \mu_h N_h(t) - \delta_h I_h(t)$$

In the absence of the disease $(\delta_h = 0)$

$$\frac{dN_h(t)}{dt} \leq \Lambda_h - \mu_h N_h(t)$$

Therefore;

$$\frac{dN_h(t)}{dt} + \mu_h N_h(t) \leq \Lambda_h \qquad (2)$$

Solving equation (2) yields;

$$N_h \leq \frac{\Lambda_h}{\mu_h} + C_1 e^{-\mu t}$$

Where C_1 is a constant of integration; applying initial conditions at $t = 0$

$N_h \leq \frac{\Lambda_h}{\mu_h} + (N_h(0) - \frac{\Lambda_h}{\mu_h})e^{-\mu t} \qquad (3)$

Using the theorem of differential inequality, we obtain

$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h}$ as $t \to \infty$

Thus as $t \to \infty$ in equation (3), the human population N_h approaches $k = \frac{\Lambda_h}{\mu_h}$. The parameter $k = \frac{\Lambda_h}{\mu_h}$ is usually called the carrying capacity.

Hence, all feasible solutions set of the human population of the model (1) enters the region

$D_h = \left\{(S_h, E_h, M_h, C_h, R_h) \in \mathbb{R}_+^5 : S_h > 0, E_h \geq 0, M_h \geq 0, C_h \geq 0, R_h \geq 0, N_h \leq \frac{\Lambda_h}{\mu_h}\right\}$

Similarly, the feasible solution set of the mosquito population enters the region;

$D_m = \left\{(S_m, E_m, I_m) \in \mathbb{R}_+^3 : S_m > 0, E_m \geq 0, I_m \geq 0, N_m \leq \frac{\Lambda_m}{\mu_m}\right\}$

Thus, the feasible solution set for the model (1) is given by:

$$D = \left\{ \begin{array}{c} (S_h, E_h, M_h, C_h, R_h S_m, E_m, I_m) \in \mathbb{R}_+^8 : (S_h, S_m) > 0, \ (E_h, M_h, C_h, R_h, E_m, I_m) > 0, \\ N_h \leq \frac{\Lambda_h}{\mu_h}, \ N_m \leq \frac{\Lambda_m}{\mu_m} \end{array} \right\}$$

Therefore, the region D is positively – invariant and the model (1) is biologically meaningful and mathematically well - posed in the domain D.

POSITIVITY OF SOLUTIONS:

It is necessary to prove that all solutions of system (1) with positive initial data will remain positive for all time $t > 0$. This will be established by the following Lemma:

Lemma 2: Let the initial data be

$\{(S_h(0), S_m(0)) > 0, \ (E_h(0), M_h(0), C_h(0), R_h(0), E_m(0), I_m) \geq 0\} \in D$, then the solution set

$\{S_h, E_h, M_h, C_h, R_h, S_m, E_m, I_m\}(t)$ of the model solution (1) is positive for all $t > 0$.

Proof: From the first equation of system (1), we have;

$$\frac{ds_h}{dt} = \Lambda_h + \psi R_h - (k_1 + \mu)S_h$$

$$\frac{ds_h}{dt} \geq -(k_1 + \mu)S_h$$

Integrating both sides with respect to t, we have;

$$\ln S_h \geq -\int (k_1 + \mu) \, dt + C_2$$

This implies that:

$$S_h(t) \geq e^{[-\int (k_1 + \mu)dt + C_2]}$$

$$S_h(t) \geq e^{-[\int (k_1 + \mu)dt]} \times e^{C_2}$$

At $t = 0$

$$S_h(t) \geq S_h(0)e^{-[\int k_1 dt + \mu t]}$$

Since $e^x > 0 \ \forall \ x \in \mathbb{R}$;

$$S_h(t) \geq S_h(0)e^{[-\int k_1 dt + \mu t]} \geq 0$$

Similarly from second equation of system (1), we have that;

$$\frac{dE_h}{dt} = k_1 S_h - (\alpha_h + \mu_h)E_h$$

$$\frac{dE_h}{dt} \geq -(\alpha_h + \mu_h)E_h$$

$$\int \frac{1}{E_h} dE_h \geq \int -(\alpha_h + \mu_h)dt$$

At $t = 0$

$$E_h(t) \geq E_h(0)e^{-(\alpha_h + \mu_h)t} \geq 0$$

From the third equation of (1), we also have that;

$$\frac{dM_h}{dt} = \alpha_h E_h - (\varepsilon + \tau + \mu_h)M_h$$

$$\frac{dM_h}{dt} \geq -(\varepsilon + \tau + \mu_h) M_h$$

Integrating both sides with respect to t at $t = 0$, we obtain;

$$M_h(t) \geq M_h(0)e^{-(\varepsilon + \tau + \mu_h))t} \geq 0$$

Following the above procedure, it can be shown that the remaining equations of system (1) are also positive for all $t = 0$.

EXISTENCE OF DISEASE – FREE EQUILIBRIUM POINTS:

Equilibrium points are steady state solutions of the system equation (1) when the right hand side is equal to zero. That is:

$$\left. \begin{aligned} \Lambda_h + \psi R_h - (k_1 + \mu)S_h &= 0 \\ k_1 S_h - (\alpha_h + \mu_h)E_h &= 0 \\ \alpha_h E_h - (\varepsilon + \tau + \mu_h)M_h &= 0 \\ \tau M_h - (\theta + \mu_h + \delta_h)C_h &= 0 \\ \varepsilon M_h + \theta C_h - (\psi + \mu_h)R_h &= 0 \\ \Lambda_m - b(k_2 + k_3)S_m - \mu_m S_m &= 0 \\ (k_2 + k_3)S_m - (\alpha_m + \mu_m)E_m &= 0 \\ \alpha_m E_m - \mu_m I_m &= 0 \end{aligned} \right\} \qquad (4)$$

Let $E_0 = (S_h^*, \ E_h^*, \ M_h^*, \ C_h^*, \ R_h^*, \ S_m^*, \ E_m^*, \ I_m^*)$ be the disease – free equilibrium point. Solving equation (4) when $E_h = M_h = C_h = R_h = E_m = I_m = 0$, we have;

$$E_0 = (S_h^*, \ E_h^*, \ M_h^*, \ C_h^*, \ R_h^*, \ S_m^*, \ E_m^*, \ I_m^*) = \left(\frac{\Lambda_h}{\mu_h}, \ 0, \ 0, \ 0, 0, \frac{\Lambda_m}{\mu_m}, 0, \ 0\right)$$

(5)

which represent the steady state in which there is no plasmodium parasite in the community.

BASIC REPRODUCTION NUMBER R_0

The basic reproduction number denoted by R_0 is an important parameter which is used to study the behavior of epidemiological models. Diekman et al (1990) defined the basic reproduction number as the expected number of secondary cases produced by a typical infective individual. It is an important threshold parameter that determines whether or not an infection will spread through a given population (Musa & Goni, 2018). We apply the next generation matrix technique to obtain the basic reproduction number R_0 by considering the infected compartments of system (6). That is:

$$\left.\begin{array}{c} \dot{E}_h = k_1 S_h - (\alpha_h + \mu_h)E_h \\[2mm] \dot{M}_h = \alpha_h E_h - (\varepsilon + \tau + \mu_h)M_h \\[2mm] \dot{C}_h = \tau M_h - (\theta + \mu_h + \delta_h)C_h \\[2mm] \dot{E}_m = (k_2 + k_3)S_m - (\alpha_m + \mu_m)E_m \\[2mm] \dot{I}_m = \alpha_m E_m - \mu_m I_m \end{array}\right\} \qquad (6)$$

Let $\boldsymbol{x} = \{E_h^{**}, \ M_h^{**}, \ C_h^{**}, \ E_m^{**}, \ I_m^{**}\}^T$, therefore the model (6) can be written as;

$\dot{\boldsymbol{x}} = F(x) - V(x)$, where F and V are defined as:

$$F = \begin{pmatrix} \frac{b\beta_h S_h I_m}{1+eI_m} \\[3mm] 0 \\[3mm] 0 \\[3mm] \frac{b\beta_{1m} M_h S_m}{1+eM_h} + \frac{b\beta_{2m} C_h S_m}{1+eC_h} \\[3mm] 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} (\alpha_h + \mu_h)E_h \\[3mm] (\varepsilon + \tau + \mu_h)M_h - \alpha_h E_h \\[3mm] (\theta + \mu_h + \delta_h)C_h - \tau M_h \\[3mm] (\alpha_m + \mu_m)E_m \\[3mm] \mu_m I_m - \alpha_m E_m \end{pmatrix}$$

The Jacobian matrix of F and V at the disease – free equilibrium point, E_0 gives:

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & \dfrac{b\beta_h\Lambda_h}{\mu_h} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \dfrac{b\beta_{1m}\Lambda_m}{\mu_m} & \dfrac{b\beta_{2m}\Lambda_m}{\mu_m} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} (\alpha_h + \mu_h) & 0 & 0 & 0 & 0 \\ -\alpha_h & (\varepsilon + \tau + \mu_h) & 0 & 0 & 0 \\ 0 & -\tau & (\theta + \mu_h + \delta_h) & 0 & 0 \\ 0 & 0 & 0 & (\alpha_m + \mu_m) & 0 \\ 0 & 0 & 0 & -\alpha_m & \mu_m \end{pmatrix}$$

The inverse of the Jacobian matrix V denoted by V^{-1} gives:

$$\begin{pmatrix} \dfrac{1}{(\alpha_h + \mu_h)} & 0 & 0 & 0 & 0 \\ \dfrac{\alpha_h}{(\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)} & \dfrac{1}{(\varepsilon + \tau + \mu_h)} & 0 & 0 & 0 \\ \dfrac{\alpha_h\tau}{(\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)} & \dfrac{\tau}{(\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)} & \dfrac{1}{(\theta + \mu_h + \delta_h)} & 0 & 0 \\ 0 & 0 & 0 & \dfrac{1}{(\alpha_m + \mu_m)} & 0 \\ 0 & 0 & 0 & \dfrac{\alpha_m}{\mu_m(\alpha_m + \mu_m)} & \dfrac{1}{\mu_m} \end{pmatrix}$$

Therefore, the product of the Jacobian matrix F and the inverse of V denoted by FV^{-1} yields;

$$FV^{-1} = \begin{pmatrix} 0 & 0 & 0 & a & b \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ c & d & h & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

where:

$$a = \frac{b\beta_h \Lambda_h \alpha_m}{\mu_h \mu_m (\alpha_m + \mu_m)}, \quad b = \frac{b\beta_h \Lambda_h}{\mu_h \mu_m}, \quad c = \frac{b\Lambda_m \alpha_h [\beta_{1m}(\theta + \mu_h + \delta_h) + \beta_{2m}\tau]}{\mu_m (\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)},$$

$$d = \frac{b\Lambda_m [\beta_{1m}(\theta + \mu_h + \delta_h) + \beta_{2m}\tau]}{\mu_m (\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)} \quad \text{and} \quad h = \frac{b\Lambda_m \beta_{2m}}{\mu_m (\theta + \mu_h + \delta_h)}$$

So that the spectral radius (dominant eigenvalues) of the matrix FV^{-1} is calculated from the characteristic equation; $|FV^{-1} - \lambda I| = 0$ where I is a 5×5 identity matrix: That is:

$$\begin{vmatrix} -\lambda & 0 & 0 & a & b \\ 0 & -\lambda & 0 & 0 & 0 \\ 0 & 0 & -\lambda & 0 & 0 \\ c & d & h & -\lambda & 0 \\ 0 & 0 & 0 & 0 & -\lambda \end{vmatrix} = 0 \qquad (7)$$

Solving for $\lambda_i, i = 1, 2, 3, 4, 5$ in equation (7) and substituting for a, b, c, d, h. we have;

$$\lambda_i = \begin{pmatrix} 0 \\ 0 \\ 0 \\ -\sqrt{\dfrac{b^2 \beta_h \Lambda_h \Lambda_m \alpha_h \alpha_m [\beta_{1m}(\theta + \mu_h + \delta_h) + \beta_{2m}\tau]}{\mu_h \mu_m^2 (\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)(\alpha_m + \mu_m)}} \\ \sqrt{\dfrac{b^2 \beta_h \Lambda_h \Lambda_m \alpha_h \alpha_m [\beta_{1m}(\theta + \mu_h + \delta_h) + \beta_{2m}\tau]}{\mu_h \mu_m^2 (\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)(\alpha_m + \mu_m)}} \end{pmatrix}$$

But $R_0 = \rho(FV^{-1})$, hence;

$$R_0 = \sqrt{\frac{b^2 \beta_h \Lambda_h \Lambda_m \alpha_h \alpha_m [\beta_{1m}(\theta + \mu_h + \delta_h) + \beta_{2m}\tau]}{\mu_h \mu_m^2 (\alpha_h + \mu_h)(\varepsilon + \tau + \mu_h)(\theta + \mu_h + \delta_h)(\alpha_m + \mu_m)}} \tag{8}$$

NUMERICAL EXPERIMENT

In this section, the behavior of system (1) is investigated numerically using some of the parameter values compactible with malaria as given in table 3 below. The numerical experiment was perfumed using MATLAB software with the following initial conditions: $S_h(0) = 1000$, $E_h(0) = 20$, $M_h(0) = 10$, $C_h(0) = 0$, $R_h(0) = 0$, $S_m(0) = 10000$, $E_m(0) = 20$ and $I_m(0) = 30$

Table 3: MODEL PARAMETER VALUES

Parameters	Values	Parameters	Values
ϕ	0.05	b	0.12
τ	0.4	β_h	0.032
θ	0.05	β_{1m}	0.048
Λ_h	0.000215	β_{1m}	0.48
Λ_m	0.07	α_h	$^1/_{17}$
μ_h	0.0000548	α_m	18
μ_m	$^1/_5$	ψ	$^1/_{730}$
δ_h	0.001		

Sources: Aguilar & Gutierrez (2020); Bala & Gimba (2019); Otieno, Koske & Mutiso (2016);

Olaniyi & Obabiyi (2013). Chitnis,(2005).

The numerical experiment accessed the impact of the control measure (the use of anti – malaria herbal therapy as first – line treatment of mild malaria infection) incorporated in system (1) as shown in figure 2 below. It is observed that the number of complicated infectious human population decline significantly as a result of the control measure.
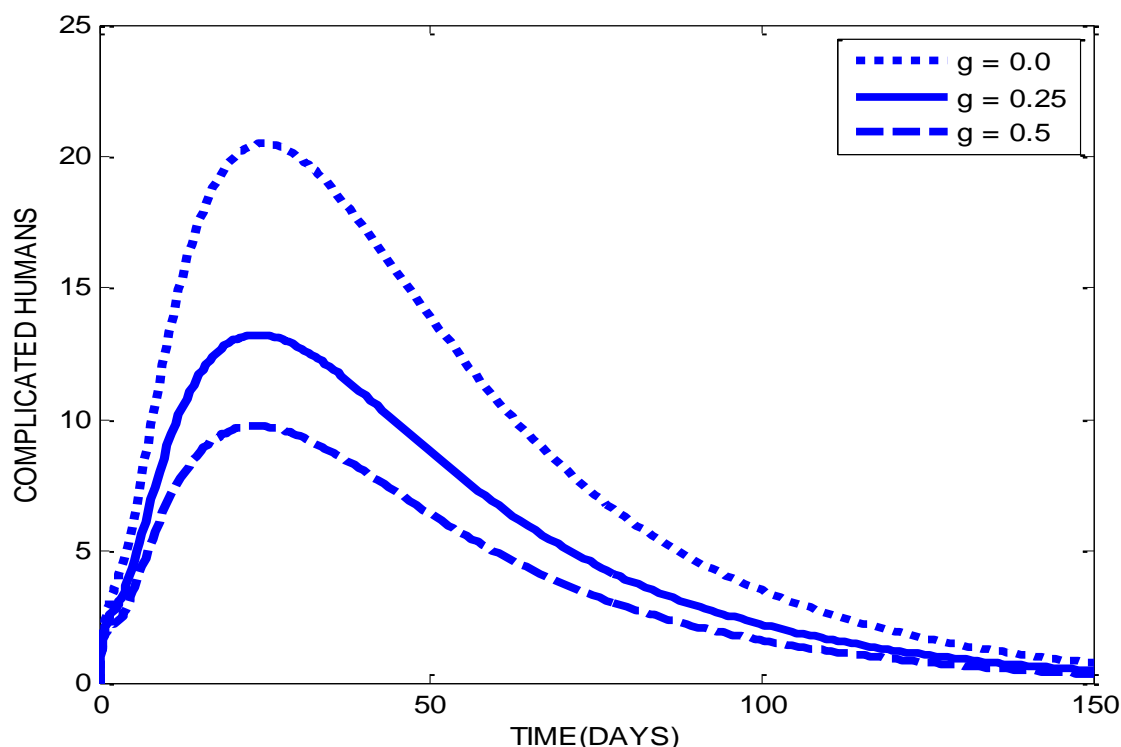
Figure 2: The behaviour of complicated human compartment at different parameter values of g (per capita rate of recovery due to anti – malarial herbal therapy) while other parameters remain unchanged

CONCLUSION AND RECOMMENDATIONS

A mathematical model of malaria transmission was formulated considering the mild (uncomplicated) and severe (complicated) malaria infection cases in different compartments. The progression of mild cases to severe infection is considered to be treatment failure and the absence of some genetic factors in host population. Anti-malarial herbal therapy which serves as first – line treatment for uncomplicated malaria infection was incorporated in the model as the control measure. The region where the model is epidemiological feasible and mathematically well – posed was established and the basic reproduction number R_0 was explicitly derived using the next generation matrix approach. Numerical experiment was conducted to access the impact of the control measure, result shown in figure 2 revealed that the control measure will drastically reduce malaria burden in region where the level of compliance is high unlike areas with poor level of compliance.

We therefore suggest massive campaign on the use of anti-malarial herbal therapy for first-line treatment of mild malaria infection cases, as *plasmodium* parasites have developed resistance to most malaria drugs.

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