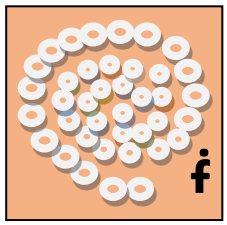

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The influence of aquatic mosquitoes on Lymphatic Filariasis transmission dynamics: mathematical model approach

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Abstract

The disease burden of lymphatic filariasis (LF) is a concern worldwide as it is one of the leading causes of permanent disability. In this study, a mathematical model of lymphatic filariasis is formulated with interest in the aquatic mosquito population (egg, larva and pupa) on the metamorphosis of the mosquito life cycle. The existence of the disease-free and the endemic equilibrium states and the basic reproduction number are established. In addition, the sensitivity indices indicate that the biting rate of mosquitoes, the recruitment rate of the aquatic mosquito population, the probability of transmitting infection during contact between humans and mosquitoes and the mortality rate of mosquitoes are the sensitive parameters in the disease dynamics. Through numerical simulations, it is observed that the sensitive parameters have an effect in reducing the burden of lymphatic filariasis in the population. Thus, public health education and the usage of larvicides should be encouraged as these would cause a drastic reduction in the maturation rate of mosquitoes, especially in communities where stagnant waters are endemic.

Keywords: Lymphatic Filariasis; aquatic mosquitoes; basic reproduction number; sensitivity analysis

1 Introduction

Lymphatic filariasis (LF), also called elephantiasis, is a neglected tropical disease whose causative agent are filaria worms, and it infects the lymphatic system [1]. LF is categorised into acute and chronic stages, and about 1.4 billion persons worldwide are at risk of infection [2]. The disease is transmitted via mosquitoes from one person to another, and infected persons can suffer from elephantiasis [3]. Lymphatic filariasis is a public health challenge in developing countries, even though the knowledge of drug usage is high. The relationship between lymphatic filariasis and humans depends on the filaria worms, external conditions and mosquitoes [4], [5]. One of the ways to control diseases caused by mosquitoes is to control the mosquito population. Thus, understanding the mosquito life cycle dynamics is important [6]. An important parameter affecting the mosquito population's size is the availability of breeding sites as it influences its life cycle [7]. The life cycle of a mosquito is categorised into four clearly different stages of progression: egg, larva, pupa and adult in its lifetime. They are completely distinct, even in habitation and ecology. After sucking blood from its victims, non-aquatic female mosquitoes lay a large amount of eggs in stagnant or slow-moving water. In less than seven days, larvae emerge from the egg, breathing through tubes that protrude above the water surface. They feed on floating organic matter and practise cannibalism. The larvae shed part of their bodies four times in the growth process and metamorphosed into pupae. The habitat of the pupa is close to the water's surface, and respiration occurs through the siphons on their back. The pupae stage of the life cycle does not feed until the skin splits and an adult mosquito emerges. The egg, larva and pupa stages are aquatic stages. In contrast, the adult stage is the non-aquatic stage in the metamorphosis of mosquitoes, and each has different responses to the environment and regulating factors to the population [8], [9] and [6]. Thus,

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to improve our understanding of the dynamics of lymphatic filariasis concerning the mosquito vector, we need to include the age structure to determine the appropriate mosquito population targeted for control strategies.

Several mathematical models that analyse the dynamics of lymphatic filariasis abound. Even though some have limitations, none of them has considered the influence of the aquatic mosquito on lymphatic filariasis disease. For instance, Mwamtobe *et al.* [10] considered quarantine of infected individuals as a strategy for reducing the transmission of lymphatic filariasis while Oguntolu *et al.* [11] considered treatment as a control measure for lymphatic filariasis. Simelane *et al.* [12] examined the application of indoor residual spraying to non-aquatic or adult mosquitoes while Salonga *et al.* [13], Rychta and Taylor [14] introduced mass drug administration for persons so that the disease could be eliminated. In addition, Stephano *et al.* [15] suggested that the recruitment rate of mosquitoes positively influences the spread of lymphatic filariasis. Hence, the aquatic mosquito compartment (eggs, larvae and pupa stages), which influences the rate of recruitment of the non-aquatic mosquito population (adult stage), is introduced in this study since ecological interactions among aquatic mosquitoes are crucial because they influence egg hatching, competition and population density [16].

The remaining part considers the formulation of the model in Section 2, qualitative analysis of the model in Section 3, while Numerical simulations with discussion and conclusion are presented in Section 4.

2 Model formulation

The total human population, N_h, at any time t, is subdivided into susceptible human, S_h, exposed human, E_h, asymptomatic infected human, I_{1h}, and symptomatic infected human, I_{2h}. The population of susceptible humans is generated by recruitment or birth at a constant rate of Λ_h and treatment of individuals in the asymptomatic human class at a rate, α. Proportion of this individuals acquires filariasis infection following effective contact with infectious mosquitoes, I_m, at the rate of λ_h where $\lambda_h = \frac{\beta\theta_1 I_m}{N_h}$, is the force of infection with β as mosquito biting rate and θ_1 as the probability that a bite from infected mosquito results in an infection. Humans exit this class due to natural death rate, μ_h; this is given by

$$\frac{dS_h}{dt} = \Lambda_h - \lambda_h S_h - \mu_h S_h + \alpha I_{1h}.$$

Humans in the exposed class, E_h, are recruited from the susceptible human class with contact with an infected mosquito. Exposed humans exit the class at a rate, τ, to the asymptomatic human class when the contact results in an infection or due to a natural death rate, μ_h. The rate of change of the exposed humans is given by

$$\frac{dE_h}{dt} = \lambda_h S_h - (\tau + \mu_h)E_h.$$

Members of the asymptomatic infected human class, I_{1h}, are recruited from the E_h class at a rate τ and exit this class to the susceptible human class due to treatment at a rate, α, or via natural death rate, μ_h. Some proceeds to the symptomatic human class due to lack of treatment at a rate, η. This yields

$$\frac{dI_{1h}}{dt} = \tau E_h - (\alpha + \mu_h + \eta)I_{1h}.$$

The symptomatic human class comprises humans who do not pay attention to health instructions, and they are recruited from the asymptomatic human class, I_{1h}, at a rate, η. They exit the class as a result of natural death rate, μ_h, or disease-induced death rate, δ. Thus,

$$\frac{dI_{2h}}{dt} = \pi I_{1h} - (\delta + \mu_h)I_{2h}.$$

The mosquito population comprises aquatic and non-aquatic mosquitoes. The population of aquatic mosquitoes is divided into eggs, larvae, and pupae, while the non-aquatic mosquito population is divided into susceptible mosquitoes, S_m, and infected mosquitoes, I_m. The aquatic mosquito population

increases through oviposition by reproductive mosquitoes at the rate, Λ, and they exit this class through maturation at a rate, ϕ, or by death rate, μ_l. This yields

$$\frac{dL}{dt} = \Lambda - (\phi + \mu_l)L.$$

The susceptible mosquitoes are recruited from the aquatic mosquito class due to maturation, and they exit this class due to death rate, μ_m, or as a result of infection when they come in contact with infected humans. The dynamics of this class are given by

$$\frac{dS_m}{dt} = \phi L - \lambda_m S_m - \mu_m S_m,$$

with $\lambda_m = \frac{\beta\theta_2(I_{1h}k+I_{2h})}{N_h}$, where θ_2 is the probability that a contact with an infected human result in an infection and k accounts for the reduced adult microfilariae due to treatment.

Finally, the population of infectious mosquitoes, I_m, is generated by the progression of mosquitoes from the susceptible mosquito class when they come in contact with infected humans at a rate, λ_m, and they exit this class as a result of death rate, μ_m. Thus,

$$\frac{dI_m}{dt} = \lambda_m S_m - \mu_m I_m.$$

It is assumed that the mosquito does not die of the disease.
Using the above information and the model schematic diagram, the non-linear system of equations is derived as below.

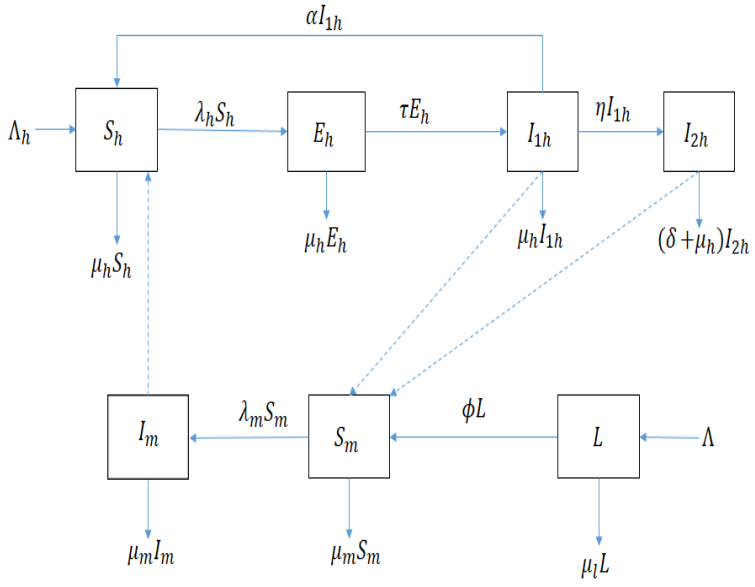

Figure 1: Schematic diagram of the lymphatic filariasis model

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h - \lambda_h S_h - \mu_h S_h + \alpha I_{1h}, \\
\frac{dE_h}{dt} &= \lambda_h S_h - (\tau + \mu_h) E_h, \\
\frac{dI_{1h}}{dt} &= \tau E_h - (\alpha + \mu_h + \eta) I_{1h}, \\
\frac{dI_{2h}}{dt} &= \eta I_{1h} - (\delta + \mu_h) I_{2h}, \\
\frac{dL}{dt} &= \Lambda - (\phi + \mu_l) L, \\
\frac{S_m}{dt} &= \phi L - \lambda_m S_m - \mu_m S_m, \\
\frac{dI_m}{dt} &= \lambda_m S_m - \mu_m I_m,
\end{aligned}\right\} \tag{1}$$

subject to initial conditions $S_h(0) > 0$, $E_h(0) \geq 0$, $I_{1h}(0) \geq 0$, $I_{2h}(0) \geq 0$, $L > 0$, $S_m(0) > 0$, $I_m(0) \geq 0$ where $\lambda_h = \frac{\beta\theta_1 I_m}{N_h}$ and $\lambda_m = \frac{\beta\theta_2(kI_{1h}+I_{2h})}{N_h}$. The system (1) is assumed to have positive model parameters.

The following Table 1 shows the parameter values of the lymphatic filariasis model.

Table 1: Values of parameters used in simulation.

Parameter	Symbol	Value	Source
Human recruitment rate	Λ_h	2500	[10]
Human mortality rate	μ_h	0.039	[10]
Human disease-induced death rate	δ	0.1	Assumed
Treatment rate for I_{1h} class	α	0.619	[13]
Movement rate from the E_h to the I_{1h} class	τ	0.25	[12]
Movement rate from the I_{1h} to the I_{2h} class	η	0.35	[12]
Aquatic mosquito maturity rate	ϕ	0.6	Assumed
Non-aquatic mosquito mortality rate	0.166	μ_m	[1]
Aquatic mosquito recruitment rate	Λ	40000	Assumed
Aquatic mosquito mortality rate	μ_l	0.019	[17]
Reduction parameter for I_{1h} due to treatment	k	0.055	[10]
Mosquito biting rate	β	0.3	[1]
Transmission rate for interaction between S_h and I_m class	θ_1	0.64	[17]
Transmission rate for interaction between S_m and I_{1h}, I_{2h} class	θ_2	0.64	[17]

3 Analysis of the model

3.1 Invariant region

The model parameters are assumed to be non-negative with non-negative initial conditions, implying that the model is biologically meaningful. The system of equations (1) will be analysed in a suitable feasible region, obtained as follows.

Let the total human population, $N_h(t) = S_h(t) + E_h(t) + I_{1h}(t) + I_{2h}(t)$, the aquatic mosquito population, $L(t)$, and the total non aquatic mosquito population $N_m(t) = S_m(t) + I_m(t)$, at time $t > 0$ have initial conditions $N_h(0)$= N_{h0}, $L(0)$ = L_0, and $N_m(0) = N_{m0}$ respectively. We state the following lemma.

Lemma 3.1. *All feasible solutions are uniformly bounded in a proper subset*

$$\varphi = \varphi_h \times \varphi_l \times \varphi_m$$

where

$$\varphi_h = \left\{ (S_h, E_h, I_{1h}, I_{2h}) \in \Re_+^4 : N_h(t) \leq \frac{\Lambda_h}{\mu_h} \right\}, \ \varphi_l = \left\{ L\epsilon\Re_+ : L(t) \leq \frac{\Lambda}{\phi + \mu_l} \right\}$$

and

$$\varphi_m = \left\{ (S_m, I_m)\epsilon\Re_+^2 : N_m(t) \leq \frac{\phi\Lambda}{\mu_m(\phi + \mu_l)} \right\}$$

are subsets for human, aquatic mosquitoes and non-aquatic mosquito populations, respectively.

Proof. It is assumed without loss of generality that disease-induced death rate, δ, in the human class in Equation (1) is negligible; that is, adding all human sub-populations to get

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h N_h - \delta I_{2h} \ \leq \ \Lambda_h - \mu_h N_h. \tag{2}$$

Applying Birkhoff and Rota [18] theorem on differential inequality and integrating both sides of (2), we have after simplifying that

$$N_h \leq \frac{\Lambda_h}{\mu_h} - \left[\frac{\Lambda_h - \mu_h N_{h0}}{\mu_h} \right] e^{-\mu_h t}. \tag{3}$$

As $t \longrightarrow \infty$ in (3), the human population size, $N_h \longrightarrow \frac{\Lambda_h}{\mu_h}$. Therefore, all feasible regions of the human populations, S_h, E_h, I_{1h}, and I_{2h} enter the region

$$\varphi_h = \left\{ (S_h, E_h, I_{1h}, I_{2h}) \in \Re_+^4 : N_h(t) \leq \frac{\Lambda_h}{\mu_h} \right\}.$$

For the aquatic mosquito population, we have

$$\frac{dL}{dt} = \Lambda - (\phi + \mu_l)L. \tag{4}$$

Applying Birkhoff and Rota [18] theorem of differential inequality and integrating both sides of (4) using the initial condition, $L(0) = L_0$ results to

$$L \leq \frac{\Lambda}{\mu_l + \phi} - \left[\frac{\Lambda - (\mu_l + \phi)L_0}{\mu_l + \phi} \right] e^{(-\mu_l + \phi)t}. \tag{5}$$

As $t \longrightarrow \infty$ in (5), the aquatic mosquito population size, L approaches $\frac{\Lambda}{\mu_l + \phi}$. Thus, the feasible regions of the aquatic mosquito populations, L, will enter the region

$$\varphi_l = \left\{ L\epsilon\Re_+ : L(t) \leq \frac{\Lambda}{\phi + \mu_l} \right\}.$$

Since the non-aquatic mosquito population, $N_m(t)$, does not suffer from disease-induced death, we have

$$\frac{dN_m}{dt} = \phi L - \mu_m N_m. \tag{6}$$

Applying Birkhoff and Rota [18] theorem on differential inequality and integrating both sides of (6) with $L(t) \leq \frac{\Lambda}{\phi + \mu_l}$, we have

$$N_m \leq \frac{\phi\Lambda}{\mu_m(\mu_l + \phi)} - \left[\frac{\phi\Lambda - \mu_m(\mu_l + \phi)N_{m0}}{\mu_m(\mu_l + \phi)} \right] e^{-(\frac{\phi\Lambda}{\mu_m(\mu_l + \phi)})t}. \tag{7}$$

As $t \longrightarrow \infty$ in (7), the non-aquatic mosquito population size, $N_m \longrightarrow \frac{\phi\Lambda}{\mu_m(\mu_l + \phi)}$. Therefore, all feasible regions of the non-aquatic mosquito populations, S_m and I_m, enter the region

$$\varphi_m = \left\{ (S_m, I_m) \in \Re_+^2 : N_m(t) \leq \frac{\phi\Lambda}{\mu_m(\mu_l + \phi)} \right\}.$$

This implies that every solution with an initial condition in $\Re_+^6$ remains in that region for $t > 0$, which is a positively invariant set under the flow induced by the model (1). Thus, the system (1) is epidemiologically meaningful and mathematically well-posed in the domain's interior, φ. Therefore, in this domain, it is sufficient to consider the dynamics of the flow generated by the model (1).

3.2 Positivity of solutions

Since φ is a positive invariant set, we now show that for $t > 0$, every solution of the model is positive and remains in the region.

Theorem 3.2. *The closed set*

$$D = \Big\{ \Big(S_h(t), E_h(t), I_{1h}(t), I_{2h}(t), L(t), S_m(t), I_m(t) \Big) \in \mathbb{R}^7_+ : N_h(t) \leq \frac{\Lambda_h}{\mu_h}, L(t) \leq \frac{\Lambda}{\phi + \mu_l}, \\ N_m(t) \leq \frac{\phi\Lambda}{\mu_m(\mu_l + \phi)} \Big\}$$

is positively invariant and attracts all positive solutions of the model (1) where $N_h(t)$ is the human population size, L(t) is the aquatic mosquito population and $N_m(t)$ is the non-aquatic mosquito population at any time t, respectively.

Proof. Let $\tau = sup\{t > 0 : S_h(0) > 0, I_{1h}(0) > 0, I_{2h}(0) > 0, L(0) > 0, S_m(0) > 0, I_m(0) > 0\}\epsilon[0, t]$.

From the first Equation in (1), we have

$$\frac{dS_h}{dt} = \Lambda_h - \lambda_h S_h - \mu_h S_h + \alpha I_{1h} \geq -(\lambda_h + \mu_h)S_h.$$

This implies by integration with initial condition, $S_h(0)$, that

$$S_h \geq S_h(0) exp\{-(\mu_h + \int_0^t \lambda_h(u))t\} > 0.$$

This shows that S_h is always positive for $t > 0$.

In similar way for $t > 0$,

$$E_h(t) \geq E_h(0) \exp -(\tau + \mu_h)t > 0, \;\; I_{1h}(t) \geq I_{1h}(0) \exp -(\alpha + \eta + \mu_h)t > 0,$$

$$I_{2h}(t) \geq I_{2h}(0) \exp -(\mu_h + \delta)t > 0, \;\; L(t) \leq L(0) \exp -(\phi + \mu_l) > 0,$$

$$S_m(t) \geq S_m(0) exp\{-\int_0^t (\lambda_m + \mu_m) du\} > 0, \;\; I_m(t) \geq I_m(0) \exp(-\mu_m)t > 0.$$

Therefore, we can conclude that the solutions

$$(S_h(t), E_h(t), I_{1h}(t), I_{2h}(t), L(t), S_m(t), I_m(t))$$

of model Equation (1) are non-negative for $t > 0$. This implies the model is well-positioned and makes biological meaning because we cannot have negative sub-populations for living organisms.

3.3 Disease-free equilibrium state and basic reproduction number

The disease-free equilibrium (DFE) is the steady-state solution of the system of equations (1) obtained in the absence of disease, that is, $E_h = I_{1h} = I_{2h} = I_m = 0$. Thus, the disease-free equilibrium state E_0, is given by

$$E_0 = \Big(S_h^0, 0, 0, 0, L^0, S_m^0, 0 \Big) = \Big(\frac{\Lambda_h}{\mu_h}, 0, 0, 0, \frac{\Lambda}{\phi + \mu_l}, \frac{\phi\Lambda}{\mu_m(\phi + \mu_l)}, 0 \Big). \tag{8}$$

3.3.1 Basic reproduction number

The basic reproduction number, R_0, is the number of new cases reproduced in a wholly susceptible population when an infective individual is introduced into the population (Van den Driessche and Watmough, [19]). We apply the next-generation approach by Van den Driessche and Watmough, [19], [20]. The next generation matrix comprises two parts: F and V, where $F = \frac{\partial f_i(E_0)}{\partial x_j}$ and $V = \frac{\partial v_i(E_0)}{\partial x_j}$. Also, the f_i are the new infections while the v_i are transfers of infections from one compartment to another with E_0 as a disease-free equilibrium state. R_0 is the the spectral radius of the matrix FV^{-1} with the associated matrix F and matrix V as Jacobian matrices of f_i and v_i at disease-free equilibrium state, E_0.

The Jacobian matrix F and V and the inverse of matrix V are given as

$$F = \begin{pmatrix} 0 & 0 & 0 & \beta\theta_1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & k\beta\theta_2 a_4 & \beta\theta_2 a_4 & 0 \end{pmatrix}, V = \begin{pmatrix} a_1 & 0 & 0 & 0 \\ -\tau & a_2 & 0 & 0 \\ 0 & -\eta & a_3 & 0 \\ 0 & 0 & 0 & \mu_m \end{pmatrix} \text{ and } V^{-1} = \begin{pmatrix} \frac{1}{a_1} & 0 & 0 & 0 \\ \frac{\tau}{a_1 a_2} & \frac{1}{a_2} & 0 & 0 \\ \frac{\eta\tau}{a_1 a_2 a_3} & \frac{\eta}{a_2 a_3} & \frac{1}{a_3} & 0 \\ 0 & 0 & 0 & \frac{1}{\mu_m} \end{pmatrix}$$

where

$$a_1 = \tau + \mu_h, a_2 = \alpha + \eta + \mu_h, a_3 = \delta + \mu_h, a_4 = \frac{S_m^0}{N_h^0} = \frac{\Lambda\phi\mu_h}{\Lambda_h\mu_m(\phi + \mu_l)}, a_6 = \phi + \mu_l. \quad (9)$$

The spectral radius (dominant eigenvalue) of FV^{-1},which is the basic reproduction number R_0 is given by

$$R_0 = \rho(FV^{-1}) = \sqrt{\frac{\beta^2 a_4\theta_1\theta_2\tau(a_3k + \eta)}{a_1a_2a_3\mu_m}}.$$

With the definition in Equation in (9), we have

$$R_0 = \sqrt{\frac{\beta^2\theta_1\theta_2\tau\Lambda\phi\mu_h(k(\delta + \mu_h) + \eta)}{(\tau + \mu_h)(\alpha + \eta + \mu_h)(\delta + \mu_h)\mu_m^2\Lambda_h(\phi + \mu_l)}}. \quad (10)$$

Interpretation of the basic reproduction number

The biological interpretation of the basic reproduction number, R_0, is as follows:

- $\frac{\tau}{\tau+\mu_h}$ is the probability of survival of the individuals from the exposed state to the infectious state,
- $\frac{\theta_1\beta}{\mu_m^2}$ is the number of humans that one mosquito infects during the duration of the infectious period, provided all humans are susceptible,
- $\frac{\theta_2\beta}{(\alpha+\eta+\mu_h)(\delta+\mu_h)}$ is the number of mosquitoes that a human infects during the duration of the infectious period, provided all mosquitoes are susceptible,
- $\frac{\beta\theta_2\Lambda\phi}{\mu_m^2(\phi+\mu_l)}$ is the contribution of the mosquito population when humans are infected,
- $\frac{\beta\theta_1\tau(k(\delta+\mu_h)+\eta)}{(\tau+\mu_h)(\alpha+\eta+\mu_h)(\delta+\mu_h)\Lambda_h)}$ is the contribution of the human population when mosquitoes are infected.

The square root is the geometric mean of the average number of new infections produced by one mosquito and the average number of new infections produced by a human. Thus, R_0 could be written as

$$R_0 = \sqrt{(R_{1h} + R_{2h})R_m}, \quad (11)$$

where

$R_m = \frac{\beta\theta_1}{\mu_m}$ is the reproduction number resulting from the interaction of susceptible humans and infected mosquitoes,

$R_{1h} = \frac{\beta\theta_2\tau\Lambda\phi\mu_h k(\delta+\mu_h)}{(\tau+\mu_h)(\alpha+\eta+\mu_h)(\delta+\mu_h)\mu_m\Lambda_h(\phi+\mu_l)}$ is the reproduction number resulting from the interaction of asymptomatic infected humans and susceptible mosquitoes,

$R_{2h} = \frac{\beta\theta_2\tau\Lambda\phi\mu_h\eta}{(\tau+\mu_h)(\alpha+\eta+\mu_h)(\delta+\mu_h)\mu_m\Lambda_h(\phi+\mu_l)}$ is the the basic reproduction number resulting from the interaction of symptomatic infected humans and susceptible mosquitoes.

3.4 Stability of the disease-free equilibrium state

3.4.1 Local stability of the disease-free equilibrium state

The local stability of the DFE depends on the basic reproduction number, R_0, as proved by Van den Driessche and Watmough [19]. The linearization method at the equilibrium state is used to establish the local stability of the DFE. We state and prove the following theorem.

Theorem 3.3. *If E_0 is the DFE of the model, then E_0 is locally asymptotically stable if $R_0 < 1$, but unstable if $R_0 > 1$.*

Proof. The Jacobian matrix of the model (1) at DFE, E_0, is given by

$$J(E_0) = \begin{pmatrix} -\mu_h & \alpha & 0 & 0 & 0 & 0 & -\beta\theta_1 \\ 0 & -a_1 & 0 & 0 & 0 & 0 & \beta\theta_1 \\ 0 & \tau & -a_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & \eta & -a_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -a_6 & 0 & 0 \\ 0 & 0 & -\beta\theta_2 k a_4 & -\beta\theta_2 a_4 & \phi & -\mu_m & 0 \\ 0 & 0 & \beta\theta_2 k a_4 & \beta\theta_2 a_4 & 0 & 0 & -\mu_m \end{pmatrix}.$$

The eigenvalues of the Jacobian matrix, $J(E_0)$, are $-\mu_h$, $-\mu_m$, $-a_6$ and the roots of the polynomial

$$\lambda^4 + A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0,$$

where

$$\begin{aligned} A_3 &= \mu_m + a_3 + a_2 + a_1, \\ A_2 &= a_1a_2 + a_1a_3 + a_1\mu_m + a_2a_3 + a_2\mu_m + a_3\mu_m, \\ A_1 &= a_1a_2a_3 + a_1a_3\mu_m + a_2a_3\mu_m + a_1a_2\mu_m\left(1 - \frac{\beta^2 k\tau\theta_1\theta_2 a_4 a_5}{a_1a_2\mu_m}\right), \\ A_0 &= a_1a_2a_3\mu_m\left(1 - \frac{\beta^2\theta_1\theta_2\tau a_4a_5(ka_3+\eta)}{a_1a_2a_3\mu_m}\right). \end{aligned}$$

Writing the coefficients of the polynomial in terms of the basic reproduction number yields

$$A_1 = a_1a_2a_3 + a_1a_3\mu_m + a_2a_3\mu_m + a_1a_2\mu_m(1 - R_{1h}),\ A_0 = a_1a_2a_3\mu_m\left(1 - R_0^2\right).$$

Thus, the stability of the disease-free equilibrium of the model (1) is determined solely by the sign of the constant term of the characteristic equation where all parameters are non-negative. Also, A_1, A_2, A_3 has the property that $A_0, A_1, A_2, A_3 > 0$. Hence, we can conclude that the eigenvalues of the system have negative real parts if $R_0 < 1$, therefore, the DFE, E_0, is locally asymptotically stable if $R_0 < 1$.

3.4.2 Global stability of the disease-free equilibrium state

The global stability of disease-free equilibrium is established using the Comparison theorem by Castillo-Chavez *et al.* [21]. We state the following theorem for the global stability of the DFE E_0.

Theorem 3.4. *The DFE E_0 of the model equations (1) is globally asymptotically stable if $R_0 \leq 1$ and unstable if $R_0 > 1$.*

Proof. The first condition is to define new variables and rewrite the system into subsystems.

Let X_1 and Y_1 represent susceptible and infectious classes, respectively. The subsystems of the model equations (1) gives $X_1 = (S_h, L, S_m)$ and $Y_1 = (E_h, I_{1h}, I_{2h}, I_m)$ which could be represented as

$$\left.\begin{aligned} \frac{dX_1}{dt} &= F(X_1, Y_1), \\ \frac{dY_1}{dt} &= G(X_1, Y_1), \end{aligned}\right\} \tag{12}$$

with $X_1 \in \mathbb{R}^3_+, Y_1 \in \mathbb{R}^4_+$. The two vector value functions are

$$\left.\begin{aligned} F(X_1, Y_1) &= (\Lambda_h - \lambda_h S_h - \mu_h S_h + \alpha I_{1h},\ \Lambda - (\phi + \mu_l)L,\ \phi L - \lambda_m S_m - \mu_m S_m)^T, \\ G(X_1, Y_1) &= (\lambda_h S_h - (t + \mu_h)E_h,\ \tau E_h - (\alpha + \mu_h + \eta)I_{1h},\ \eta I_{1h} - (\delta + \mu_h)I_{2h},\ \lambda_m S_m - \mu_m I_m)^T, \end{aligned}\right\}$$

where T is the transpose, $\lambda_h = \frac{\beta\theta_1 I_m}{N_h}$, and $\lambda_m = \frac{\beta\theta_2(I_{1h}k + I_{2h})}{N_h}$.

The reduced system, $\frac{dX_1}{dt}F(X_1, 0)$, in the absence of disease is given as

$$\left.\begin{aligned} \frac{dS_h}{d_t} &= \Lambda_h - \mu_h S_h, \\ \frac{dL}{dt} &= \Lambda - (\phi + \mu_l)L, \\ \frac{dS_m}{d_t} &= \phi L - \mu_m S_m. \end{aligned}\right\} \tag{13}$$

with the Jacobian matrix $\begin{pmatrix} -\mu_h & 0 & 0 \\ 0 & -a_6 & 0 \\ 0 & \phi & -\mu_m \end{pmatrix}$.

The Jacobian matrix has the eigenvalues $-\mu_h, -a_6$ and $-\mu_m$. The equilibrium state of the $\frac{dX_1}{dt}F(X_1, 0)$, in the absence of disease is $X^* = (S_h^*, L^*, S_m^*) = (\frac{\Lambda_h}{\mu_h}, \frac{\Lambda}{\phi + \mu_l}, \frac{\phi\Lambda}{\mu_m(\phi + \mu_l)})$ and it is globally asymptotically stable, which implies that the reduced system does not dependent on the initial conditions in $\mathbb{R}^7_+$.

Condition 2 states that $G(X_1, Y_1) = AY - G^*(X_1, Y_1)$, where $G(X_1, Y_1) \geq 0$ for $X_1, Y_1 \in \varphi$ and $A = D_Y G(X^*, 0)$ is an M-matrix. Form the model system (1),

$$A = D_Y G(X_1, 0) = \begin{pmatrix} -a_1 & 0 & 0 & \beta\theta_1 \\ \tau & -a_2 & 0 & 0 \\ 0 & \eta & -a_3 & 0 \\ 0 & \beta k\theta_2 a_4 & \beta\theta_2 a_4 & -\mu_m \end{pmatrix} \text{ and } G^*(X_1, Y_1) = \begin{pmatrix} \beta\theta_1 I_m \left(\frac{S_h^0}{N_h^0} - \frac{S_h}{N_h}\right) \\ 0 \\ 0 \\ \beta\theta_2 I_{2h} \left(\frac{S_m^0}{N_h^0} - \frac{S_m}{N_h}\right) \end{pmatrix},$$

where $G(X_1, Y_1)$ satisfies $G(X_1, 0) = 0$. We observed that $G(X_1, Y_1) = A^* Y_1 - G^*(X_1, Y_1)$, and $G^*(X_1, Y_1) \geq 0$ since $\frac{S_h^0}{N_h^0} \geq \frac{S_h}{N_h}$, $\frac{S_m^0}{N_h^0} \geq \frac{S_m}{N_h}$. Therefore by Castillo-Chavez *et al.* [21], X^* is a globally asymptotically stable state of the model equations (1) of which $R_0 < 1$ makes matrix A an M-matrix.

3.5 Endemic equilibrium state

The endemic equilibrium (EE) is an equilibrium state in the presence of the disease. At the endemic equilibrium state, E_e, the infected compartments are not equal to zero implying that $\lambda_h \neq 0$ and

$\lambda_m \neq 0$. Solving the model equations (1) in terms of the force of infection, λ_h and λ_m gives

$$\left.\begin{aligned} S_h^e &= \frac{a_2\Lambda_h - (a_1a_2 - \alpha\tau)E_h^e}{a_1\mu_h},\ E_h^e = \frac{\Lambda_h a_2\lambda_h^e}{\mu_h a_1 a_2 + (a_1a_2 - \alpha\tau)\lambda_h^e},\ I_{1h}^e = \frac{\tau E_h^e}{a_2}, \\ I_{2h}^e &= \frac{\eta I_{1h}^e}{a_3},\ L^e = \frac{\Lambda}{a_6},\ S_m^e = \frac{\phi L^e}{\lambda_m^e + \mu_m},\ I_m^e = \frac{\lambda_m^e S_m^e}{\mu_m},\ N_h^e = \frac{\Lambda_h - \delta I_{2h}^e}{\mu_h}. \end{aligned}\right\} \tag{14}$$

Substituting (14) into $\lambda_m^e = \frac{\beta\theta_2(kI_{1h}^e + I_{2h}^e)}{N_h^e}$ and $\lambda_h^e = \frac{\beta\theta_1 I_m^e}{N_h^e}$ and solve simultaneously to get

$$\lambda_m^e = \frac{C\lambda_h^e}{B\lambda_h^e + D}$$

and λ_h^e as the solution of the polynomial

$$\lambda_h^e(M_2\lambda_h^{e2} + M_1\lambda_h^e + M_0) = 0 \tag{15}$$

where

$$M_2 = \mu_m a_6\Lambda_h B(\mu_m B + C),\ M_1 = \mu_m a_6\Lambda_h D(\mu_m B + C - \mu_m\delta\eta\tau + \mu_m a_3 A(1 - R_0^2)),$$
$$M_0 = \mu_h\mu_m^2 D a_1a_2a_3a_6\Lambda_h(1 - R_0^2),$$

with

$$A = a_1a_2 - \alpha\tau > 0,\ B = a_3A - \delta\eta\tau > 0,\ C = \tau\beta\theta_1\mu_h(ka_3 + \eta),\ D = \mu_h a_1a_2a_3.$$

From the polynomial (15), it is either

$$\lambda_h^e = 0 \tag{16}$$

or

$$M_2\lambda_h^{e2} + M_1\lambda_h^e + M_0 = 0. \tag{17}$$

Equation (16) corresponds to the disease-free equilibrium (DFE) while we determine the existence of the possible number of endemic state(s) of the polynomial (17). Using Descartes's rule of signs with regards to the value of R_0, the result of the number of positive endemic state(s) are summarised in Table 2.

Table 2: Number of positive endemic states

M_2	M_1	M_0	Range of R_0	Number of possible positive real roots
+	+	-	$R_0 > 1$	1
+	-	-	$R_0 > 1$	1
+	+	+	$R_0 < 1$	0
+	+	+	$R_0 < 1$	2

From Table 2, we have $R_0 > 1$ for the existence of a unique positive endemic state. Meanwhile, $R_0 < 1$ may create no endemic state or two endemic states that will co-exist with the disease-free equilibrium, E_0 leading to a backward bifurcation at $R_0 = 1$. Plotting the polynomial in Equation (17) yields a forward bifurcation plot in Figure 2, which implies the existence of a unique endemic equilibrium that is stable when $R_0 > 1$.

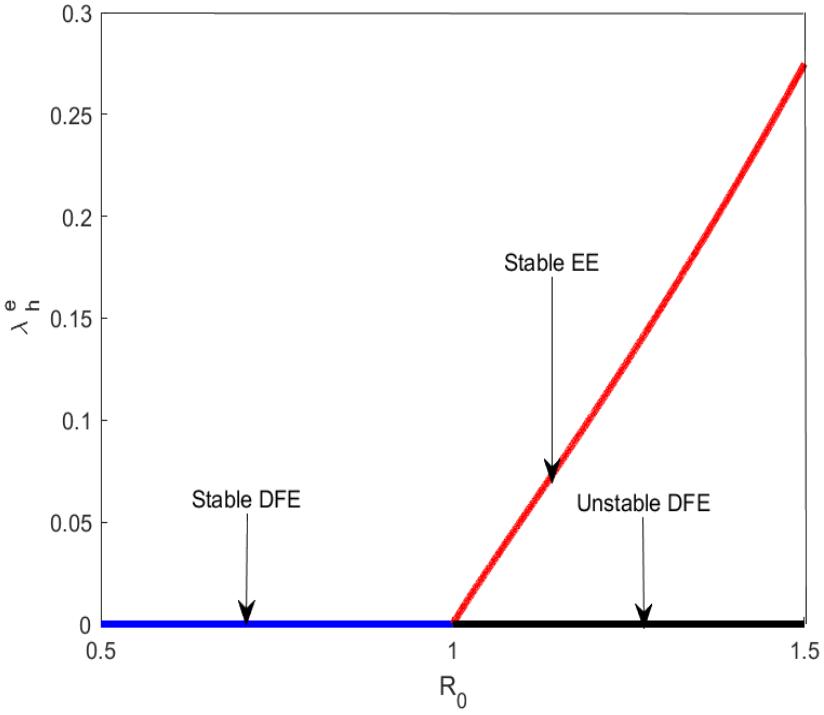

Figure 2: Plot for forward bifurcation of the Lymphatic Filariasis model at basic reproduction number R_0 using the parameter values in Table 1.

4 Numerical simulations/sensitivity analysis

4.1 Sensitivity Analysis

To determine the parameters to be targeted for intervention strategies to reduce the spread of LF disease, we need to understand the influence of the model parameters in the system concerning the flow of infection. Thus, we would conduct the sensitivity analysis on the basic reproduction number. This is carried out using the normalised forward sensitivity indices given by

$$\Gamma_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0}, \tag{18}$$

where p is any parameter of the R_0 [22]. The sensitivity indices of parameters of the basic reproduction number, R_0, are shown in Figure 2.

The sensitivity indices of the influence of the model parameters on the basic reproduction number show that mortality rate for non-aquatic mosquito population, μ_m, recruitment rate for aquatic mosquito population, Λ, mosquito biting rate, β, probability that interaction with an infected mosquito result in disease transmission, θ_1, and probability that contact with infected human results in LF disease transmission, θ_2, are sensitive parameters implying that they have an impact on the value of the basic reproduction number, R_0. In particular, mosquito biting rate, β, and mortality rate for non-aquatic mosquitoes, μ_m, are the most sensitive parameters with sensitivity indices of $+1$ and -1 respectively. It follows that β, μ_m, θ_1, θ_2 and Λ should be targeted for intervention strategies.

The 3D plots for the most sensitivity parameters are shown in Figure 4. It could be observed from the contour plots that the influence of the non-aquatic mosquito death rate, μ_m, with the mosquito biting rate, β, the recruitment rate for aquatic mosquitoes, Λ, the disease transmission rate, θ_1, and the maturity rate of mosquitoes, ϕ, on the basic reproduction number increases irrespective of the mortality rate of the non-aquatic mosquito population, μ_m. Thus, this supports the usage of larvicides to be paramount in reducing the maturity rate of mosquitoes, leading to a reduction in the mosquito

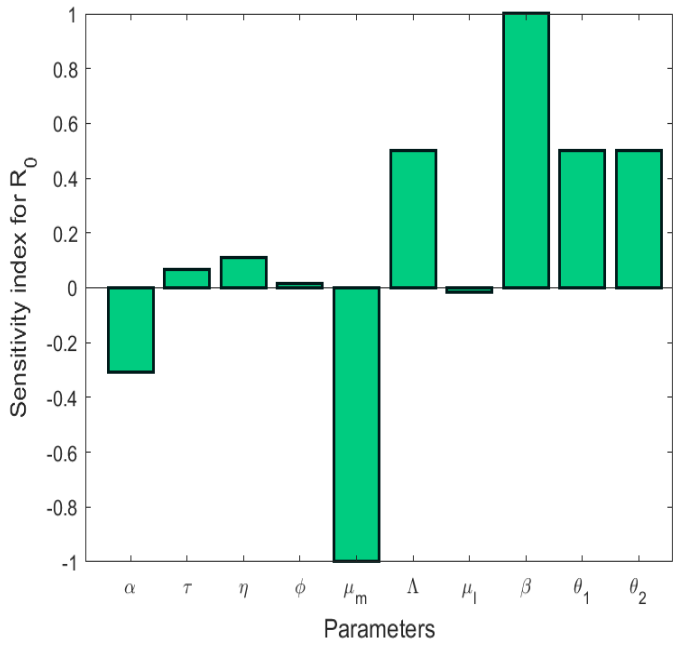

Figure 3: Sensitivity index plot of the parameters of the basic production number, R_0, using the parameter values in Table 1.

biting rate, probability of transmission and recruitment of aquatic mosquitoes.

5 Numerical Simulations

Numerical simulations of the model are carried out to investigate the behaviour of the sensitive parameters arising from the sensitivity analysis result. The parameter values in Table 1 are used for the simulations. The model is simulated by introducing one infected mosquito at the DFE of the system based on the definition of R_0.

Figure 5 shows the effect of increasing the aquatic mosquito recruitment rate, Λ. It illustrates that an increase in Λ causes an increase in infected humans and aquatic mosquito populations, contributing to the burden of LF disease in the community. In Figure 6, we observe a sharp increase in the infected human and mosquito populations when there is an increase in mosquito biting rate, β, which would cause an increase in the basic reproduction number, R_0. Furthermore, there are effects of the human transmission rate, θ_1, mosquito transmission rate, θ_2 and mosquito mortality rate, μ_m, on the spread of the LF disease in Figures 7, 8 and 9, respectively. It could be seen that an increase in θ_1 and θ_2 increases the LF burden while an increase in μ_m reduces the burden of LF in the population.

6 Discussions and Conclusion

In Figure 5 for recruitment rate for aquatic mosquitoes, $\Lambda = 60000$, there is a sharp increase in the infected human and mosquito populations in less than day 200 of the simulation as compared to $\Lambda = 40000$ and $\Lambda = 20000$ respectively. It implies that control measures like larvicide application in the environment, especially stagnant waters, should be encouraged to mitigate the maturation of aquatic mosquitoes. For Figure 6, we notice an increase in the biting rate of mosquitoes causes an increase in the number of infected humans and mosquitoes in the first 100 days of disease invasion in the population while at a reduced biting rate, say $\beta = 0.3$, it takes a longer time. The implication is that interventions such as public enlightenment campaigns on using larvicides in the environment should be encouraged to reduce the maturation of aquatic mosquitoes. It is known that the fewer mature mosquitoes in the

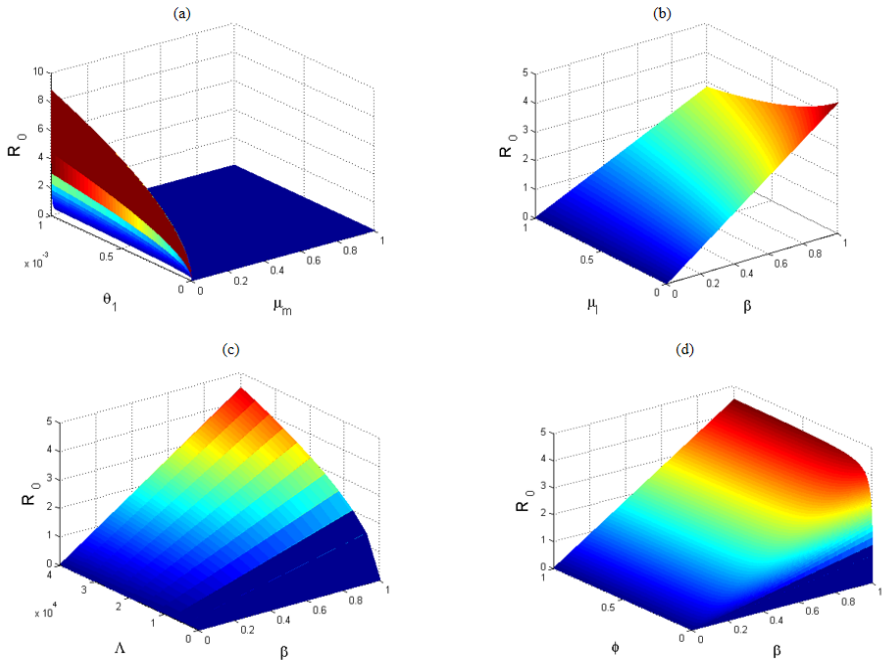

Figure 4: Contour plots showing the influence the non-aquatic mosquito death rate (μ_m), with mosquito biting rate (β), recruitment rate for aquatic mosquitoes, (Λ) disease transmission rate, (θ_1), death rate for aquatic mosquitoes, (μ_l), and maturity rate for aquatic mosquitoes, (ϕ).

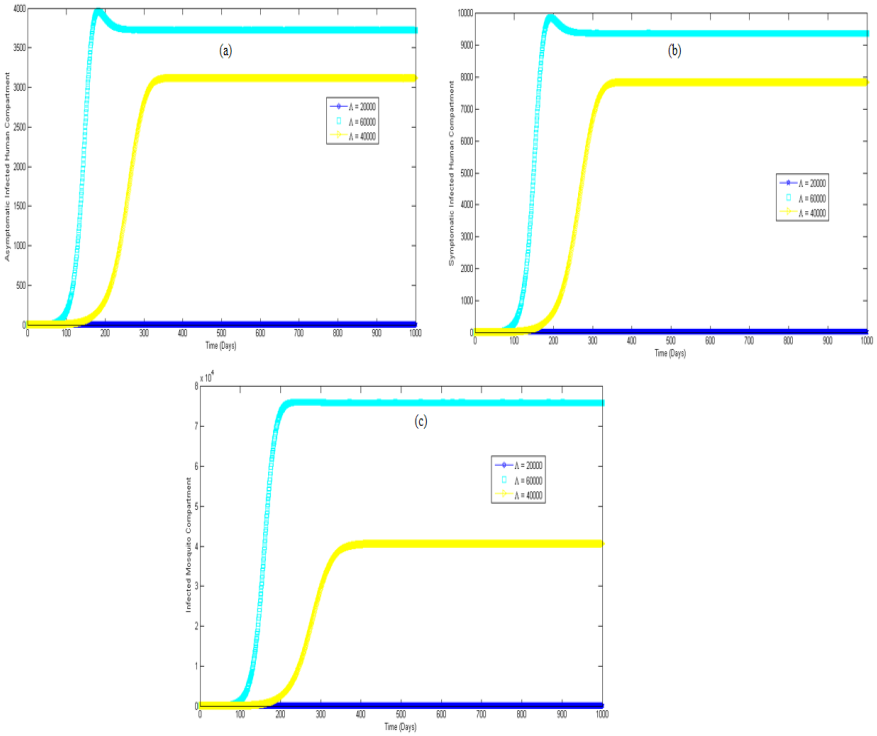

Figure 5: The influence of varying the aquatic mosquito recruitment rate (Λ) on the infective humans $(I_{1h}(t) + I_{2h}(t))$, the aquatic mosquito $(L(t))$ and the infected mosquito $(I_m(t))$ populations.

environment, the lower the biting rate of mosquitoes will lead to fewer mosquitoes in the community. Figures 7 and 8 show a geometric increase in the infected human and mosquito populations in the first 200 days when θ_1, $\theta_2 \geq 0.64$, respectively. Meanwhile, for θ_1 θ_2 equal to $= 0.44$, an increase in the

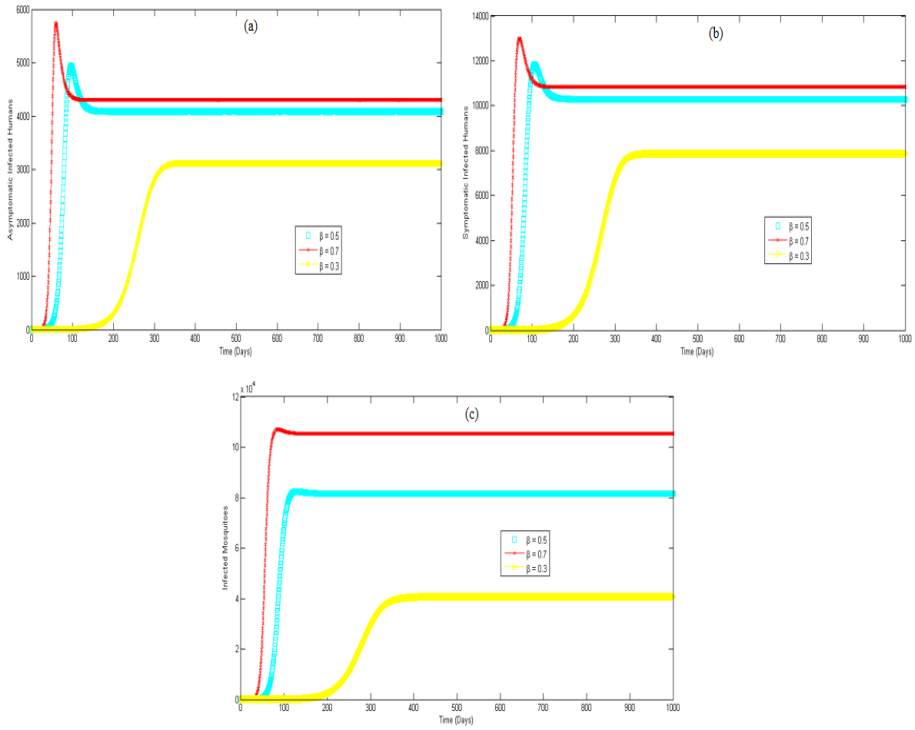

Figure 6: The influence of varying the biting rate of the non-aquatic infected mosquito (β) on the infective humans $(I_{1h}(t) + I_{2h}(t))$, the aquatic mosquito $(L(t))$ and the infected mosquito $(I_m(t))$ populations.

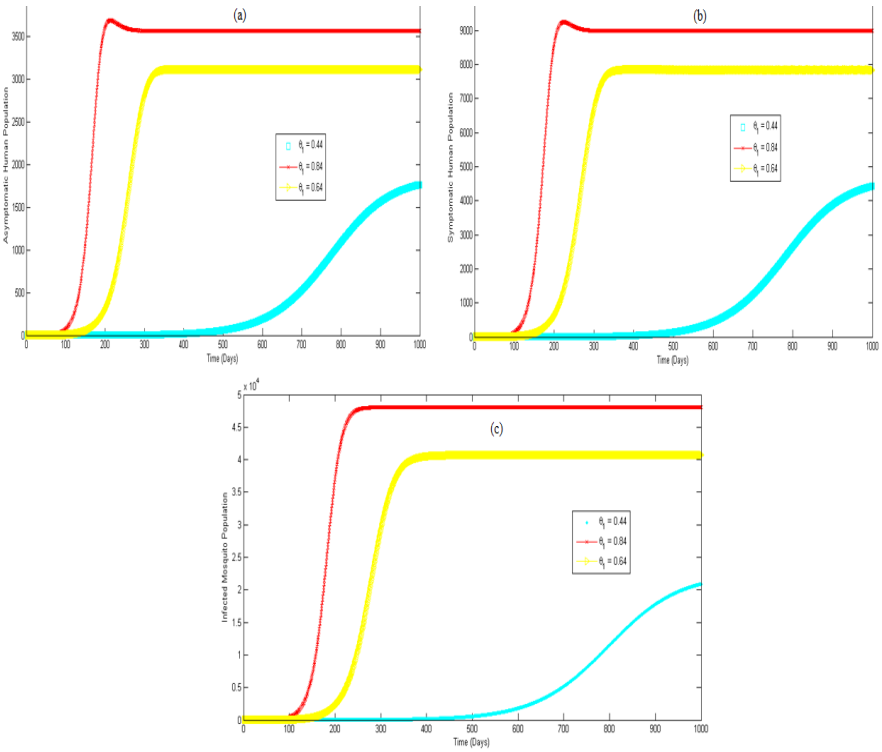

Figure 7: The influence of varying the human transmission rate (θ_1) on the infective humans $(I_{1h}(t) + I_{2h}(t))$, the aquatic mosquito $(L(t))$ and the infected mosquito $(I_m(t))$ populations.

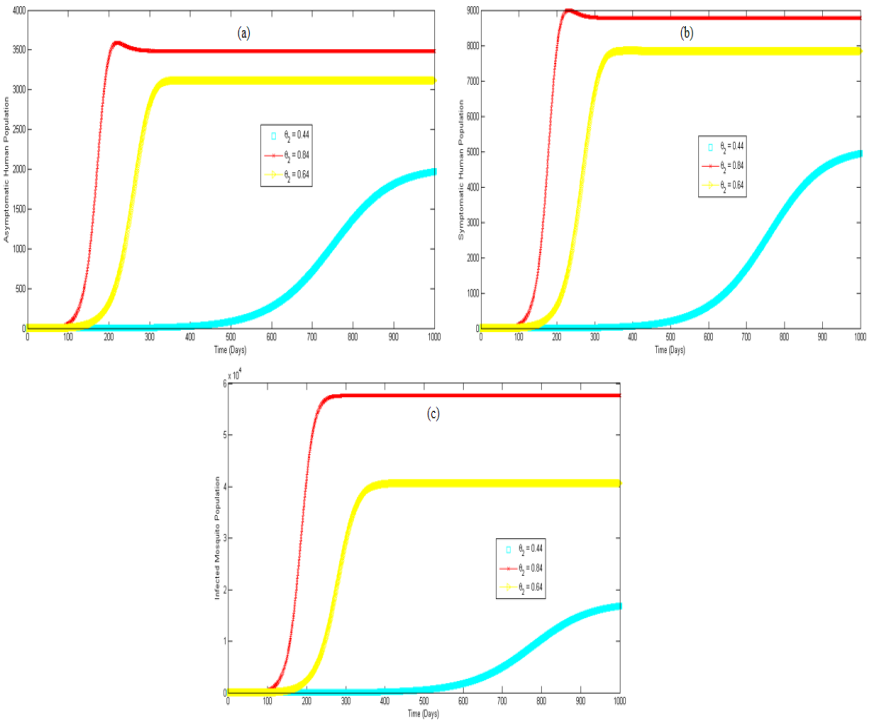

Figure 8: The influence of varying the mosquito transmission rate (θ_2) on the infective humans $(I_{1h}(t)+I_{2h}(t))$, the aquatic mosquito $(L(t))$ and the non-aquatic infected mosquito $(I_m(t))$ populations.

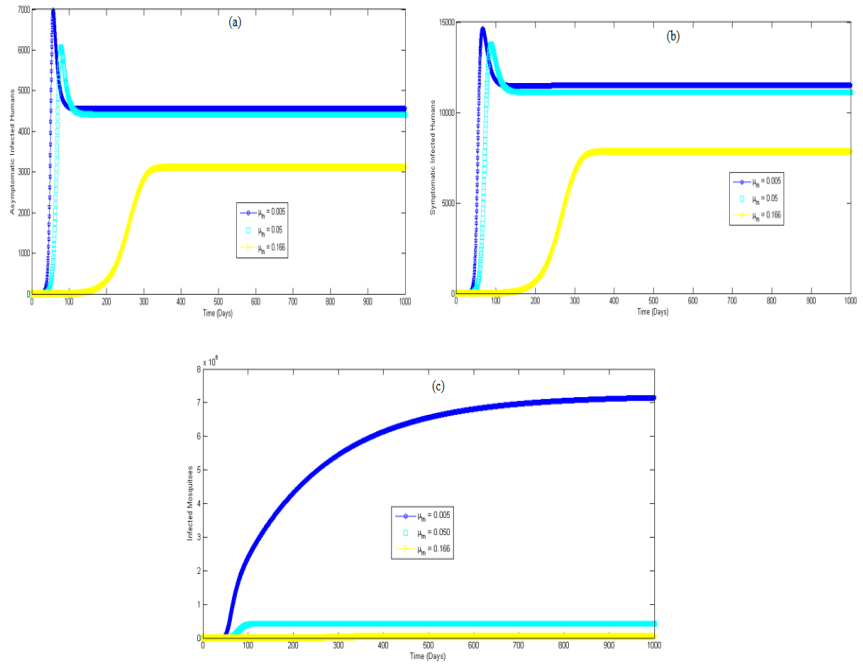

Figure 9: The influence of varying the aquatic mosquito death rate (μ_l) on the infective humans $(I_{1h}(t) + I_{2h}(t))$, the aquatic mosquito $(L(t))$ and the non-aquatic infected mosquito $(I_m(t))$ populations.

infected compartments begins in about day 600 of LF invasion. This implies that using larvicides to prevent the maturation of mosquitoes is an essential tool to reduce the probability of contact between humans and mosquitoes as it would reduce the number of mature mosquitoes in the environment. Figure 9 shows a reduction in the mortality rate of mosquitoes, causing a sharp increase in the infected human and the infected mosquito populations in less than day 100 of LF invasion. This poses a great danger to the lives of humans as the disease burden is on the rise. Thus, control measures such as public health education on the use of larvicides to eliminate the aquatic mosquito population, indoor residual spraying, and insecticide-treated bed nets are encouraged to promote the mortality rate of mosquitoes.

In conclusion, the impact of aquatic mosquitoes on the transmission dynamics of LF is studied. This involves formulating a mathematical model of LF with aquatic mosquito sub-population and conducting quantitative analysis such as computation of R_0, existence of equilibrium states and stability of disease-free equilibrium state. Furthermore, the sensitivity analysis and numerical simulations are examined in the study. Based on the result, public enlightenment campaigns should be set in motion in communities where lymphatic filariasis is endemic so that sensitisation of individuals on the usage of larvicides, insecticides-treated bed nets, indoor residual spraying as well as treatment of infected individuals should be emphasized to avoid symptomatic human cases that promote poor self-esteem among victims. Further studies could focus on modifying or extending this work to cater for individuals migrating from non-endemic areas to endemic areas and the influence of seasonality conditions to advance the understanding of the dynamics of lymphatic filariasis.

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