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Asymptotic Properties and Sensitivity Analysis for Lymphatic Filariasis Model

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Abstract: A deterministic model for the transmission dynamics of Lymphatic Fifilariasis (LF) is formulated and analyszed. By using suitable Lyapunov functions and LaSalles invariance principle, we prove the global asymptotic stability of the all equilibria of the model. It is shown that the model has a globally-asymptotically stable disease-free equilibrium whenever the threshold value called the reproductive number (R_0) is less than unity. If $R_0>1$, the model has a unique endemic equilibrium and it is locally asymptotically stable in the interior of the feasible region and the disease will persist at the endemic equilibrium if it is initially present. The sensitivity analysis based on the mathematical technique has been performed to determine the importance of the model parameters in making strategies for controlling LF.

INTRODUCTION

Lymphatic filariasis, commonly known as elephantiasis is one of the world's most disabling and dis guring diseases. This disease caused by infection with nematodes (roundworms) of the family Filariodidea[1, 2]. Currently, 856 million people in 52 countries worldwide remain threatened by lymphatic filariasis and require preventive chemotherapy to stop the spread of this parasitic infection[3]. The disease is concentrated in tropical and subtropical areas of the world, particularly Africa, India and Southeast Asia such as Myanmar. Although treatment of human populations with anti larial drugs has become the mainstay of lymphatic filariasis control[4]. This disease still be endemic, if the controlling of people who infect filariasis parasite is not efficient, elephantiasis will be a public health problem, especially in Thailand. Predicting the risk of outbreaks or the risk of patients with infectious disease[5-7] are crucial for planning, developing surveillance, preventing and control of parasitic disease elephantiasis to be appropriate to the situation that will occur in the future.

Mathematical model in epidemiology is one useful tool in providing a better knowledge of disease in order to predict the spread of infectious disease, to plan for the future course of an outbreak and to consider appropriate strategies to control an epidemic[8]. In recent year, a few of authors have studied mathematical models for the transmission of lymphatic filariasis (see, for instances[6, 9-11]. Michael *et al*.[9] reviewed recent work on the development and application of a deterministic mathematical model of filariasis transmission to suggest two key factors: the need to maintain high community treatment coverages and the need to include vector control measures, especially in areas of high endemicity, to achieve filariasis control. Bhunu and Mushayabasa[6] presented a mathematical model of lymphatic filariasis model with quarantine and treatment. They proved the

local stability of equilibria of the model and suggested that treatment contributes to a reduction in lymphatic filariasis cases faster than quarantine. Michael and Bundy[10] studied the transmission intensity and the immunoepidemiology of bancroftian filariasis in East Africa by using mathematical model together with analysis of standardized field data from communities with varying parasite transmission intensities. Jambulingam *et al*.[12] studied the lymphatic filariasis elimination programmes in India by using mathematical model and suggested the requirement duration of mass drug administration and post-treatment level of infection indicators. However, those researchs not much has been done in the rigorous qualitative analyses of the models (talkless the global stability of the model) in order to investigate the cause of disease transmission before suggesting the strategy of disease control and prevention. This study, therefore, aims to formulate a mathematical model to gain insight the transmission dynamics of lymphatic filariasis.

MATERIALS AND METHODS

Lymphatic filariasis model: Infection Lymphatic filariasis occurs when filarial parasites are transmitted to humans through the Culex mosquito. People get lymphatic filariasis from the bite of an infected mosquito. The microscopic worms pass from the skin to the lymph vessels. In the lymph vessels they grow into adults. An adult worm lives for about 57 years. The adult worms mate and release millions of microscopic worms, called micro-filariae, into the blood. People with the worms in their blood can give the infection to others through mosquitoes. For symptoms of lymphatic filariasis, Lymphatic filariasis infection involves asymptomatic, acute and chronic conditions. Most infected people are asymptomatic and will never develop clinical symptoms, despite the fact that the parasite damages the lymph system. A small percentage of persons will develop lymphedema. This is caused by improper functioning of the lymph system that results in fluid collection and swelling. This mostly affects the legs but can also occur in the arms, breasts and genitalia. Most people develop these clinical manifestations years after being infected. For these reasons, the model is formulated based on assuming a homogenous mixing of the human and mosquito populations, so that, each mosquito bite has equal chance of transmitting the virus to susceptible human in the population and acquiring infection from an infected human. The dynamics of human and mosquito populations are described as follows.

Human population: The total human population is divided into six sub-populations of Susceptible human $S_h(t)$, Treated human $T_h(t)$, Exposed human $E_h(t)$, asymptomatic human $I_{ha}(t)$, chronic human $I_{hc}(t)$ and recovered human $R_h(t)$, respectively, so that:

$$N_h(t) = S_h(t)+T_h(t)+E_h(t)+I_{ha}(t)+I_{hc}(t)+R_h(t)$$

In our model contains the population of treated humans because of WHO[3] recommends preventive chemotherapy strategy called Mass Drug Administration (MDA). MDA involves administering an annual dose of medicines to the entire at-risk population. The medicines used have a limited effect on adult parasites but effectively reduce the density of micro filariae in the bloodstream and prevent the spread of parasites to mosquitoes. According to this strategy, measures to control the disease which will focus on the treatment of large groups of people in the same area as well as all foreign workers who come to work in Thailand, by taking the drugs: Diethylcarbamazine Citrate and Albendazole (to kill the parasite) along with the treatment of all patients with parasitemia.

All newborns or immigration are assumed to be susceptible to infection and there is no vertical transmission. Thus, the recruitment of humans into susceptible class at rate Π_h. It is also assumed that all sub-populations of humans die at the same natural death rate μ_h. In addition, assuming that no death from the disease due to they are treated taking Diethycarbamzime at a rate τ_a and τ_c, respectively. Susceptible humans get lymphatic filariasis from the bite of an infected mosquito at a rate λ_h (the force of infection of humans), given by:

$$\lambda_h = \frac{bp_h I_m}{N_h}$$

Where:

b = The biting rate of vector

p_h = The transmission probability from vector to human

In controlling lymphatic filariasis, susceptible humans can protect by taking Diethylcarbamazine (DEC) every 6 mouths, then they will move to treated human at a rate δ. Treated humans infect by the bite of mosquito, then they move to exposed class at a rate $\in\lambda^*_h$. If treated human does not concern about personal care, they have a chance to become susceptible again at a rate κ.

Exposed humans develop clinical symptoms of lymphatic filariasis, they move to the asymptotic infectious class (I_{ha}) ata rate α_a and the chronic infectious class (I_{hc}) ata rate α_c, respectively. Asymptomatic and chronic humans recover by medicine treatment and move to recovered class at the rates τ_a and τ_c, respectively. Since, recovered human who have experience the disease, require continuously medicine treatment every 6 months for 2 years, thus the recovered human can move to susceptible class again at a rate γ.

Mosquito population: Recall mosquitoes never recover from infection, therefore, the total mosquito(vector) population $N_m(t)$ is divided into three sub-population: susceptible vector $S_m(t)$, exposed vector $E_m(t)$ and infectious vector $I_m(t)$, respectively, so that:

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

All newborn are assumed to be susceptible and move to susceptible class at a rate Π_m. It is also assumed that all populations of mosquitoes die at the same natural death rates μ_m. Susceptible mosquito infects by biting infected humans (asymptomatic and chronic) and move to the exposed class at a rate λ_m (the force of infection of humans), given by:

$$\lambda_m = \frac{b(p_{ma} I_{ha} + p_{mc} I_{hc})}{N_h}$$

where, p_{ma} and p_{mc} are the transmission probability from asymptotic human to vector and from chronic human to vector, respectively. Exposed mosquito develops symptoms of disease which can infect another human, and move to infected class at a rate ω.

Under above assumptions and descriptions, therefore, a mathematical model for the transmission of lymphatic filariasis is described by the following system of differential equations:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Pi_h - \frac{bp_h I_m S_h}{N_h} - \mu_h S_h + rR_h,\\
\frac{dE_h}{dt} &- \frac{bp_h I_m S_h}{N_h} - (\alpha_a + \alpha_c + \mu_h) E_h,\\
\frac{dI_{ha}}{dt} &= \alpha_a E_h - (\tau_a + \mu_h) I_{ha},\\
\frac{dI_{hc}}{dt} &= \alpha_c E_h - (\tau_c + \mu_h) I_{hac},\\
\frac{dR_h}{dt} &= \tau_a I_{ha} + \tau_c I_{hc} - (r + \mu_h) R_h,\\
\frac{dS_m}{dt} &= \Pi_m - \frac{(bp_{ma} I_{ha} + bp_{mc},\ I_{hc}) S_m}{N_h} - \mu_m S_m,\\
\frac{dE_m}{dt} &= \frac{(bp_{ma} I_{ha} + bp_{mc},\ I_{hc}) S_m}{N_h} - (\omega + \mu_m) E_m\\
\frac{dI_m}{dt} &= \omega E_m - \mu_m I_m
\end{aligned}\right\} \quad (1)$$

All parameters and state variables in the system (1) are assumed to be nonnegative due to involving human and mosquito populations. Adding the first four equations and the last three equations of system (1), we have:

$$\frac{dN_h}{dt} = \Pi_h - \mu_h N_h \text{ and } \frac{dN_m}{dt} = \Pi_m - \mu_m N_m$$

respectively. It follows that the solutions N_h and N_m of these equations approach the equilibriums Π_h/μ_h and Π_m/μ_m as $t\to\infty$, respectively. Therefore, from biological considerations, we study the system (1) in the closed set:

$$\Omega = \left\{ \begin{aligned} &(S_h, E_h, I_{ha}, I_{hc}, R_h, S_m, E_m, I_m) \in R_+^8 \,|\, S_h + E_h + \\ &I_{ha} + I_{hc} + R_h \le \frac{\Pi_h}{\mu_h}, S_m + E_m + I_m \le \frac{\Pi_m}{\mu_m} \end{aligned} \right\} \quad (2)$$

which is positively invariant with respect to (1). Existence, uniqueness and continuation results for system (1) hold in this region and all solutions starting in Ω remain there for all $t\ge 0$. Hence, the system (1) is mathematically and epidemiologically well posed[13]. Thus, it is sufficient to study the dynamics of the ow generated by the system (1) in Ω.

Analysis of the model

Disease-free equilibrium: The disease-free equilibrium of the model (1) which is obtained by setting the right hand side of the system (2.3) to zero is given by:

$$E_{01} = \left(\frac{\Pi_h}{\mu_h}, 0,\ 0,\ 0, 0,\ \frac{\Pi_m}{\mu_m}, 0, 0 \right) \quad (3)$$

According to the concept of next generation matrix and the notation in Van Den Driessche and Watmough[14]. The matrices for the new infection terms (F) and the transition terms (V) are given, respectively by:

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & bp_h \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{bp_{ma}\mu_h \Pi_m}{\Pi_h \mu_m} & \frac{bp_{mc}\mu_h \Pi_m}{\Pi_h \mu_m} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \text{ and}$$

$$V = \begin{bmatrix} Q_1 & 0 & 0 & 0 & 0 \\ -\alpha_a & Q_2 & 0 & 0 & 0 \\ -\alpha_c & 0 & Q_3 & 0 & 0 \\ 0 & 0 & 0 & Q_5 & 0 \\ 0 & 0 & 0 & -\omega & \mu_m \end{bmatrix}$$

where, $Q_1 = \alpha_a+\alpha_c+\mu_h$, $Q_2 = \tau_a+\mu_h$, $Q_3 = \tau_c+\mu_h$ and $Q_5 = \omega+\mu_m$. Further, defined $R_0 = \rho(FV^{-1})$ where ρ is the spectral radius of FV^{-1}, we get:

$$R_0 = \sqrt{\frac{b2\mu h\omega ph\Pi m\left(p_{ma}\alpha_a Q_3 + p_{mc}\alpha_c Q_2\right)}{\mu_m^2 \Pi_h Q_1 Q_2 Q_3 Q_5}} \quad (4)$$

Using Theorem 2 of Van Den Driessche and Watmough[14], the following result is established.

Lemma 3.1: The Disease-Free Equilibrium (DFE), ε_0 is Locally Asymptotically Stable (LAS) if $R_0<1$ and unstable if $R_0>1$.

This lemma indicates that R_0 is the threshold value of the model (1) called the basic reproduction number. It measures the average number of secondary infection produced that one infected population is introduced into a susceptible population[15]. In the context of epidemiology, the DFE of the model (1) is locally asymptotically stable $R_0<1$, a small influx of infected human and mosquito into the community will not generate large lymphatic filariasis outbreaks and the disease will be eradicated from the community if the initial sizes of the eight state variables are within the vicinity of ε_0. On the other hand, if the equilibrium ε_0 is globally asymptotically stable, then the disease will be eradicated from the population irrespective of the initial sizes of the four state variables which is of great public health interest.

Global stability of disease-free equilibrium: Recall the positively invariant region Ω in (2), it can be seen from the first equation of model (1) that if $S_h>\Pi_h/\mu_h$, then $dS_h/dt<0$. Furthermore, from the sixth equation of model (1), if $S_m>\Pi_m/\mu_m$, then $dS_m/dt<0$. Therefore, we consider the following feasible region for the model (1):

$$\Omega_1=\left\{\left(S_h,E_h,I_{ha},I_{hc},R_h,S_m,E_m,I_m\right)\in\Omega\,|\,S_h\le\frac{\Pi_h}{\mu_h},\,Sm\le\frac{\Pi_m}{\mu_m}\right\}$$

which is also positively invariance.

Theorem 3.2: The disease-free equilibrium E_{01} is Globally Asymptotically Stable (GAS) whenever $R_0\le1$.

Proof: If $R_0\le1$, then from Theorem 3.2, the model (1) has no positive endemic equilibrium which is located in Ω_1. Consider the Lyapunov function:

$$L(t)=G_1E_h+G_2I_{ha}+G_3I_{hc}+G_4E_m+G_5I_m$$

Where:

$$G_1=\frac{b\omega\Pi_m\left(p_{ma}\alpha_aQ_3+p_{mc}\alpha_cQ_2\right)}{\mu_mQ_1Q_2Q_3},\ G_2=\frac{b\omega p_{ma}}{\mu_mQ_2},$$
$$G_3=\frac{b\omega\Pi_mp_{mc}}{\mu_mQ_3},\ G_4=\frac{\omega\Pi_h}{\mu_h},G_5=\frac{\Pi_hQ_5}{\mu_h}$$

The derivative of L with respect to t along the solution of the model (1) is given by:

$$\begin{aligned}L'(t)&=\frac{b\omega\Pi_m\left(p_{ma}\alpha_aQ_3+p_{mc}\alpha_cQ_2\right)}{\mu_mQ_1Q_2Q_3}\left(\frac{bp_hI_mS_h}{N_h}-Q_1E_h\right)\\&+\left(\frac{b\omega p_{ma}\Pi_mQ_3}{\mu_mQ_2Q_3}\right)\left(\alpha_aE_h-Q_2I_{ha}\right)+\left(\frac{b\omega p_{mc}\Pi_mQ_2}{\mu_mQ_2Q_3}\right)\left(\alpha_cE_h-Q_3I_{hc}\right)\\&+\frac{\omega\Pi_h}{\mu_h}\left(\frac{\left(bp_{ma}I_{ha}+bp_{mc}I_{hc}\right)S_m}{N_h}-Q_5E_m\right)+\frac{Q_5\Pi_h}{\mu_h}\left(\omega E_m-\mu_mI_m\right)\\&=\frac{b\omega p_h\Pi_mI_mS_h\left(p_{ma}\alpha_aQ_3+p_{mc}\alpha_cQ_2\right)}{\mu_mQ_1Q_2Q_3N_h}-\frac{b\omega p_{ma}\Pi_mI_{ha}}{\mu_m}\\&-\frac{b\omega p_{mc}\Pi_mI_{hc}}{\mu_m}+\frac{\omega\Pi_h\left(bp_{ma}I_{ha}+bp_{mc}I_{hc}\right)S_m}{\mu_hN_h}-\frac{Q_5\mu_m\Pi_hI_m}{\mu_h}\end{aligned}$$

Since, $S_h\le N_h\le\Pi_h/\mu_h$ and $S_m\le N_m\le\Pi_m/\mu_m$, then:

$$\begin{aligned}L'(t)&\le\frac{Q_5\mu_m\Pi_h}{\mu_h}\left[\frac{b_2\mu_h\omega p_h\Pi_m\left(p_{ma}\alpha_aQ_3+p_{mc}\alpha_cQ_2\right)}{\mu_m^2\Pi_hQ_1Q_2Q_3Q_5}-1\right]I_m,\\&=\frac{Q_5\mu_m\Pi_h}{\mu_h}\left(R_0^2-1\right)I_m\end{aligned}$$

It is found that $L'\le0$ if $R_0\le1$. Furthermore, $L = 0$ if and only if $I_m = 0$. Hence, the largest invariant set in $\{(S_h, E_h, I_{ha}, I_{hc}, R_h, S_m, E_m, I_m)\in\Omega_1, L = 0\}$ when $R_0\le1$ is the singleton $\{\varepsilon_0\}$. LaSalle[16]'s invariance principle, therefore, implies that ε_0 is globally asymptotically stable in Ω_1. This completes the proof.

This theorem is indicated that the sum of the infectious human and mosquito populations vanish over time, so, the disease dies out. In next section, we show that the disease persists when $R_0>1$.

Endemic equilibrium

Existence of positive endemic equilibrium: The existence of positive endemic equilibrium of the model (1) is explored as follow. Let $\varepsilon^* = (S^*_h, E^*_h, I^*_{ha}, I^*_{hc}, R^*_h, S^*_m, E^*_m, I^*_m$ be an arbitrary endemic equilibrium at steady state. Further, let:

$$\lambda_h^*=\frac{bp_hI_m^*}{N_h^*}\text{ and }\lambda_h^*=\frac{b\left(p_{ma}I_{ha}^*+p_{mc}I_{hc}^*\right)}{N_h^*}\qquad(5)$$

be the incidence rates of human and mosquito, respectively where * represents the component of the endemic equilibrium at steady-state. Then, the state variables of the model (1) at steady state are expressed in term of λ^*_h and λ^*_m as follows:

$$S_h^* = \frac{\Pi_h Q_1 Q_2 Q_3 Q_4}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)},\ E_h^* = \frac{\Pi_h \lambda_h^* Q_2 Q_3 Q_4}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)},$$
$$I_{ha}^* = \frac{\alpha_a \Pi_h \lambda_h^* Q_3 Q_4}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)},\ I_{hc}^* = \frac{\alpha_c \Pi_h \lambda_h^* Q_3 Q_4}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)},$$
$$R_h^* = \frac{\left(Q_3\alpha_a\tau_a + Q_2\alpha_c\tau_c\right)\Pi_h\lambda_h^*}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)},\ S_m^* = \frac{\Pi_m}{\lambda_m^* + \mu_m},$$
$$E_m^* = \frac{\Pi_m\lambda_m^*}{Q_5\left(\lambda_m^* + \mu_m\right)},\ I_m^* = \frac{\omega\Pi_m\lambda_m^*}{\mu_m Q_5\left(\lambda_m^* + \mu_m\right)} \quad (6)$$

where, $C_2 = (Q_1\ Q_2+\alpha_a\ Q_3)\ \gamma+\alpha_a\ Q_2Q_3+Q_2Q_3(\alpha_c+\mu_h)$ and $Q_4 = \gamma+\mu_h$, respectively. Substituting (Eq. 6) into (Eq. 5), we get:

$$\lambda_m^* = \frac{b\Pi_h C_1 \lambda_h^*}{\mu_h\left(C_2\lambda_h^* + Q_1Q_2Q_3Q_4\right)N_h^*} \quad (7)$$

where, $C_1 = Q_3Q_4\alpha_a\ p_{ma}+Q_2Q_4\alpha_c p_{mc}$ and the value of λ^*_h is the positive solution of the equation:

$$\alpha_1\lambda_h^* + b_1 = 0 \quad (8)$$

where:

$$a_1 = \frac{bC_1 + \mu_m C_2}{\mu_m Q_1Q_2Q_3Q_4} \text{ and } b_1 = 1 - R_0^2$$

It is obvious that a_1 is always positive. On the other hand, b_1 is positive or negative depending the value of R^2_0. It is found that if $R^2_0<1$ making $b_1>0$, the linear Eq. 8 has a unique negative solution which is biologically meaningless (i.e., $\lambda^*_h<0$). When $R^2_0 = 1$, the coefficient $b_1 = 0$ making $\lambda^*_h = 0$ (corresponding to the DEF). When $R^2_0<1$, the linear Eq. (8) has a unique positive solution. Therefore, the endemic equilibrium of the model (1) is established in the following theorem.

Theorem 3.3: The model (1) has a unique endemic equilibrium, ε^*, whenever $R_0>1$ and no ε^* whenever $R_0\le 1$.

Local stability of endemic equilibrium: The local stability of endemic equilibrium ε^* of the model (1) is analyzed based on the use of the centre manifold theory[17] as described in Theorem 4.1 of Castillo-Chavez and Song[18]. To this end, let $S_h = x_1$, $E_h = x_2$, $I_{ha} = x_3$, $I_{hc} = x_4$, $R_h = x_5$, $S_m = x_6$, $E_m = x_7$ and $I_m = x_8$, so that, $N_h = x_1 +x_2+x_3+x_4+x_5$ and $N_m = x_6+x_7+x_8$, respectively. Further, by using the vector notations $x = (x_1, x_2, ..., x_8)^T$ and $f = (f_1, f_2, ..., f_8)^T$, the model (1) is written in the vector form:

$$\frac{dx}{dt} = f\left(x, \beta_h\right)$$

where, $\beta_h = bp_h$, $\beta_a = bp_{ma}$, $\beta_c = bp_{mc}$:

$$\left.\begin{aligned}
f_1 &= \Pi_h - \frac{\beta_h x_1 x_8}{x_1+x_2+x_3+x_4+x_5} - \mu_h x_1 + \gamma x_6,\\
f_2 &= \frac{\beta_h x_1 x_8}{x_1+x_2+x_3+x_4+x_5} - \left(\alpha_1+\alpha_c+\mu_h\right)x_2,\\
f_3 &= \alpha_a x_2 - \left(\tau_a+\mu_h\right)x_3,\\
f_4 &= \alpha_c x_2 - \left(\tau_c+\mu_h\right)x_4,\\
f_5 &= \tau_a x_3 + \tau_c + x_4 - (\gamma+\mu_h)x_5,\\
f_6 &= \Pi_m - \frac{\left(\beta_a x_3+\beta_c x_4\right)x_6}{x_1+x_2+x_3+x_4+x_5} + \mu_m x_6,\\
f_7 &= \frac{\left(\beta_a x_3+\beta_c x_4\right)x_6}{x_1+x_2+x_3+x_4+x_5} + \left(\omega+\mu_m\right)x_7,\\
f_8 &= \omega x_7 - \mu_m x_8
\end{aligned}\right\} \quad (9)$$

Consider the case when $R_0 = 1$ and solving for β_h, gives:

$$\beta_h = \beta_h^* = \frac{\Pi_h\mu_m^2 Q_1Q_2Q_3Q_5}{\Pi_m\mu_h\omega\left(\alpha_a\beta_a Q_3 + \alpha_c\beta_c Q_2\right)}$$

where, $\beta_h = \beta^*_h$ is chosen to be a bifurcation parameter. The Jacobian of the system (Eq. 9) evaluated at ε_0 with $\beta_h = \beta^*_h$ is given by:

$$J\left(\varepsilon_0, \beta_h^*\right) = \begin{bmatrix}
-\mu_h & \kappa & 0 & 0 & 0 & \gamma & 0 & -\beta_h^*\\
0 & -Q_1 & 0 & 0 & 0 & 0 & 0 & \beta_h^*\\
0 & \alpha_a & -Q_2 & 0 & 0 & 0 & 0 & 0\\
0 & \alpha_c & 0 & -Q_3 & 0 & 0 & 0 & 0\\
0 & 0 & \tau_a & \tau_c & -Q_4 & 0 & 0 & 0\\
0 & 0 & -\frac{\mu_h\Pi_m\beta_a}{\mu_m\Pi_h} & -\frac{\mu_h\Pi_m\beta_a}{\mu_m\Pi_h} & 0 & -\mu_m & 0 & 0\\
0 & 0 & \frac{\mu_h\Pi_m\beta_a}{\mu_m\Pi_h} & \frac{\mu_h\Pi_m\beta_a}{\mu_m\Pi_h} & 0 & 0 & -Q_5 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & \omega & -\mu_m
\end{bmatrix}$$

It follows that $J(\varepsilon_0, \beta^*_h)$ has at least one non-hyperbolic equilibrium point (i.e., the lin-earized system has at least one eigenvalue with zero real part).

Hence, the center manifold theory[17] can be used to analyze the dynamics of (1) with $\beta_h = \beta^*_h$. According to the notations and Theorem 4.1 of Castillo-Chavez and Song[18], the following computations are necessary.

The right and left eigenvectors of $J(\varepsilon_0, \beta^*_h)$ are evaluated and given by $w = [w_1, w_2, ..., w_8]^T$ and $v = (v_1, v_2, ..., v_8)$, respectively where:

$$w_1 = -\frac{\left[(\alpha_a Q_3 + \alpha_c Q_2 + Q_2 Q_3)\gamma + Q_1 Q_2 Q_3\right] w_4}{\alpha_c Q_2 Q_4},\ w_2 = \frac{Q_3 w_4}{\alpha_c},\ \frac{\alpha_a Q_3 w_4}{\alpha_c Q_2},$$

$$w_4 = w_4 > 0, w_5 = \frac{(\alpha_a \tau_a Q_3 + \alpha_c \tau_a Q_2) w_4}{\alpha_c Q_2 Q_4},\ w_6 = -\frac{\mu_h \Pi_m (\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_a Q_2) w_4}{\mu_m^2 \alpha_c \Pi_h Q_2},$$

$$w_7 = \frac{\mu_h \Pi_m (\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_a Q_2) w_4}{\mu_m \alpha_c Q_2 Q_5},\ w_8 = \frac{\omega \mu_h \Pi_m (\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_a Q_2) w_4}{\mu_m^2 \alpha_c \Pi_h Q_2 Q_5},$$

$$v_1 = v_5 = v_6 = 0,\ v_3 = \frac{\beta_a Q_1 Q_3 v_2}{\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_c Q_2},\ v_4 = \frac{\beta_c Q_1 Q_3 v_2}{\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_c Q_2},$$

$$v_7 = \frac{\mu_m \Pi_h Q_1 Q_2 Q_3 v_2}{\mu_h \Pi_m (\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_c Q_2)},\ v_8 = \frac{\mu_m \Pi_h Q_1 Q_2 Q_3 Q_5 v_2}{\omega \mu_h \Pi_m (\beta_a \alpha_a \tau_a Q_3 + \beta_c \alpha_c \tau_c Q_2)},\ v_2 = v_2 > 0$$

Further, the partial derivatives of f_i given in Eq. 9 evaluated at ε_0 and using the above expressions, it follows that:

$$\tilde{a} = \sum_{k,i\,j=1}^{8} v_k w_i w_j \frac{\partial_2 f_k}{\partial x_i \partial x_j}\left(\varepsilon_0, \beta_h^*\right) = -\frac{2\mu_h (\beta_a \alpha_a Q_3 + \beta_c \alpha_c Q_2) \xi_1 v_2 w_4^2}{\mu_m^2 \alpha_c^2 \Pi_h^2 Q_2^2 Q_4 Q_5} < 0$$

and:

$$\tilde{b} = \sum_{k,i\,j=1}^{8} v_k w_i \frac{\partial_2 f_k}{\partial x_i \partial \beta_h^*}\left(\varepsilon_0, \beta_h^*\right) = \frac{\omega \Pi_m \mu_h (\beta_a \alpha_a Q_3 + \beta_c \alpha_c Q_2) v_2 w_4}{\mu_m^2 \alpha_c \Pi_h Q_2 Q_5} > 0$$

where, $\xi_1 = \omega \mu_h \Pi_m \beta^*_h [(\alpha_a Q_3 + \alpha_c Q_2 + Q_2 Q_3)\gamma + Q_1 Q_2 Q_3] + \Pi_h \mu_m Q_1 Q_2 Q_3 Q_4 Q_5$. Clearly, ã<0 and ˜b>0. According to Theorem 3.3 and Theorem 4.1 of Castillo-Chavez and Song[18], the following theorem, therefore, is established.

Theorem 3.4: The unique endemic equilibrium ε^* of the model (1) exists and is Locally Asymptotically Stable (LAS) whenever R_0>1 and is close to 1.

RESULTS AND DISCUSSION

Sensitivity analysis: Sensitivity analysis[19] is used to determine the relative importance of the model parameter responsible for disease transmission and prevalence in order to predict the outcome of a decision which should be targeted for the strategy of disease control. Initial disease transmission is directly related to the reproductive number R_0 and disease prevalence is directly related to the endemic equilibrium point ε^*. Thus, the sensitivity indices of R_0 and ε^* of the model (1) is determined by using the following formula:

$$\varphi_p^u := \frac{p}{u} \times \frac{\partial u}{\partial p}$$

where the variable u represents R_0 and E^*, the parameter p denotes the thirteen model parameters given in Table 1.

Sensitivity indices of reproductive number: The sensitivity indices of the reproductive number R_0 to each of thirteen different parameters are evaluated at the baseline parameter values given in Table 1. The results are order form the most to least as shown in Table 2. It is noted that the negative sign means that increasing (decreasing) parameter p leads to decreasing (increasing) R_0. On the other hand, the positive sign means increasing parameter p would increase (decrease) R_0. The result in Table 2 is interpreted that, for example, φ^{R0}_{b} = +1, decreasing (or increasing) the mosquito biting rate b by 10% decreases (or increases) R_0 by 10%. Similarly, $\varphi^{R0}_{\tau c}$ = -0.455, increasing (or decreasing) the recovery rate from asymptomatic state τ_a by 10% decreases (or increases) R_0 by 4.55%. The study result in Table 2 is also

Table 1: Descriptions and values used of the model parameters of the model (1)

Parameters	Description	Nominal value (year^{-1})	References
μ_h	Natural death rate of human	0.0143	[24]
μ_m	Natural death rate of mosquito	52.1429	[24]
b	Mosquito biting rate	2400	-
p_h	Transmission probability from an infectious mosquito to a susceptible human	0.014	[23]
p_{ma}	Transmission probability from an asymptomatic human to a susceptible mosquito	0.26	[23]
p_{mc}	Transmission probability from a chronic human to a susceptible mosquito	0.2	[23]
Π_h	Human recruitment rate	147	-
Π_m	Mosquito recruitment rate	12000	-
ω	Transmission rate from E_m to Im class	30.4167	[23]
γ	Rate of loss immunity in human	5.3285	[24]
α_a	Transmission rate from E_h to I_{ha} class	1.25	[23]
α_c	Transmission rate from E_h to I_{hc} class	0.2	[23]
τ_a	Recovery rate from asymptomatic state	1.4286	[23]
τ_c	Recovery rate from chronic state	2	[23]

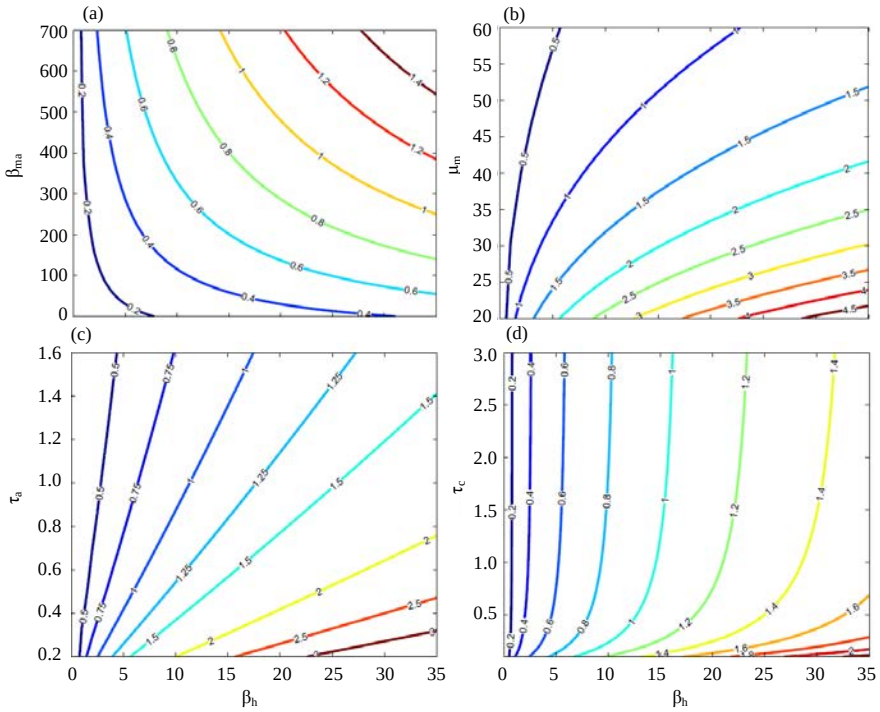

Fig. 1(a-d): The contour plot of R_0 as the function of $\beta_h = bp_h$, $\beta mc = b_{pmc}$, μ_m, τ_a and τ_c. (a) $R_0(\beta_h, \beta_{ma})$, (b) $R_0(\beta_h, \mu_m)$, (c) $R_0(\beta_h, \tau_a)$ and (d) $R_0(\beta_h, \tau_c)$

Table 2: Sensitivity indices of R_0 evaluated at the baseline parameter values

Parameters (p)	Sensitivity indices $\varphi_p^{R_0}$
μ_m	-1.316
b	+1.000
p_h	+0.500
Π_h	−0.500
Π_m	+0.500
μ_h	+0.490
p_{ma}	+0.459
τ_a	-0.455
ω	+0.316
p_{mc}	+0.041
τ_c	-0.040
α_a	+0.033
α_c	-0.028

shown that the crucial model parameters which is sensitive to R_0 consist of the sensitivity of model parameters for disease transmission are mosquito biting rate b, the transmission probability from an infectious mosquito to a susceptible human p_h, the transmission probability from an asymptomatic human to a susceptible mosquito p_{ma} and the transmission probability from a chronic human to a susceptible mosquito p_{mc}. Meanwhile, the sensitivity of model parameters for disease control are the mosquito death rate μ_m, the recovery rate from asymptomatic condition τ_a and the recovery rate from chronic condition τ_c.

To determine the effect of combination of model parameters involving disease transmission with disease control by plotting contour plot of R_0 as the function of $\beta_h = bp_h$, $\beta_{ma} = bp_{ma}$, $\beta_{mc} = bp_{mc}$, μ_m, τ_a and τ_c. The study results are displayed in Fig. 1 and 2. It is found that the reproductive number is less than unity if the model parameter involving disease transmission: b, p_h, p_{ma} and p_{mc} are decreased and the model parameter involving disease control: μ_m, τ_a and τ_c are increased. It is seen that R_0 decreases as b, p_h and p_{ma} are decreased (Fig. 1a). On the other hand, decreasing b, p_h, p_{ma} and increasing μ_m, τ_a and τ_c would decrease R_0 (Fig. 1c-d and Fig. 2a-e). Moreover, it is found that decreasing b, p_{mc} and increasing τ_c would decrease R_0 but it is not less than unity. This interprets that the treatment of patient who develops into chronic conditions is necessary but is not sufficient in eliminate the disease while treatment of patient who is asymptomatic and the effective of vector control are necessary and sufficient in eliminate the disease.

Sensitivity indices of endemic equilibrium: Similar methodology used by Chitnis *et al.*[19], the sensitivity indices for the endemic equilibrium with respect to seven model parameters are evaluated at the baseline parameter values given in Table 1. Table 3 shows the sensitivity indices for infected human and mosquito populations: I^*_{ha}, I^*_{hc} and I^*_m, respectively. It is found that the most sensitivity for I^*_{ha}, I^*_{hc} and I^*_m is the mosquito death rate μ_m and followed by b, p_h, τ_a, p_{ma}, p_{mc} and τ_c, respectively. These results are veri ed that increasing b, p_h, τ_a, p_{ma}, p_{mc}

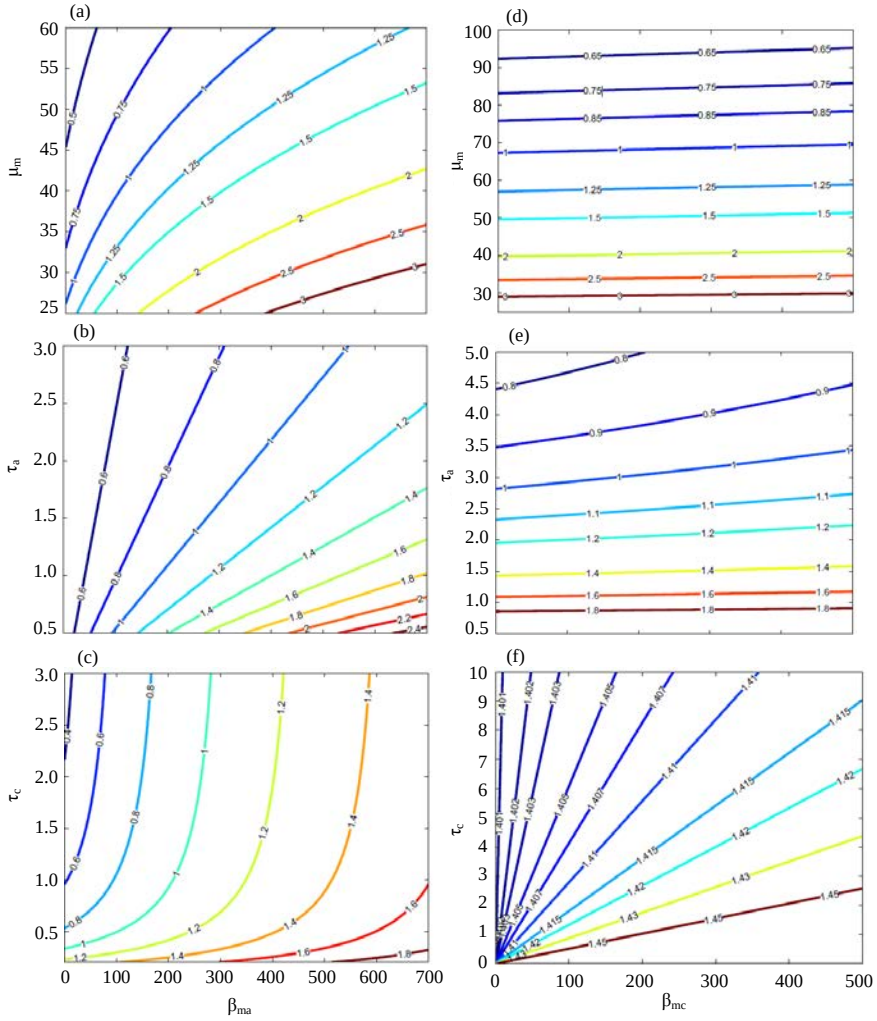

Fig. 2(a-f): Showing the contour plot of R_0 as the function of $\beta_{ma} = bp_{ma}$, $\beta_{ma} = b_{pmc}$, μ_m, τ_a and τ_c. (a) $R_0(\beta_{mc}, \mu_m)$, (b) $R_0(\beta_{mc}, \tau_a)$, (c) $R_0(\beta_{mc}, \tau_c)$, (d) $R_0(\beta_{ma}, \mu_m)$, (e) $R_0(\beta_{ma}, \tau_a)$ and (f) $R_0(\beta_{ma}, \tau_c)$

Table 3: Sensitivity indices of the point of equilibrium for human

	Sensitivity indices		
Parameters	I^*_{ha}	I^*_{hc}	I^*_m
μ_m	-3.732	-3.233	-4.517
b	+2.655	+2.300	+2.213
p_h	+1.705	+1.477	+1.064
p_{ma}	+0.872	+0.756	+1.056
p_{mc}	+0.077	+0.067	+0.093
τ_a	-1.247	-1.080	-0.233
τ_c	-0.062	-1.047	-0.084

would increase the number of infected human and mosquito populations which is the cause of disease transmission. On the other hand, increasing μ_m, τ_a and τ_c would decrease the number of infected human and mosquito populations which is the effective strategy in disease control. It is also seen that the treatment rate for asymptomatic human τa has impact to reducing the infected human and mosquito populations more than τ_c the treatment rate for chronic human τ_a. These results are verified that increasing b, p_h, τ_a, p_{ma}, p_{mc} would increase the number of infected human and mosquito populations which is the cause of disease transmission. On the other hand, increasing μ_m, τ_a and τ_c would decrease the number of infected human and mosquito populations which is the e ective strategy in disease control. It is also seen that the treatment rate for asymptomatic human τ_a has impact to reducing the infected human and mosquito populations more than τ_c the treatment rate for chronic human τ_a.

To confirm this study result, the model (1) is simulated with various τ_c: τ_c = 1.429,3.333, 10. The other model parameters used are given in Table 1. The values of τ_c corresponds to treatment regimens in controlling after 1, 3, 6 months with Diethyl-carbamazine Citrate (DEC) administration[20]. In the case when τ_c = 1.429, the number of infected human are compared with the real data in Thailand, 1994-2005. It is found that the

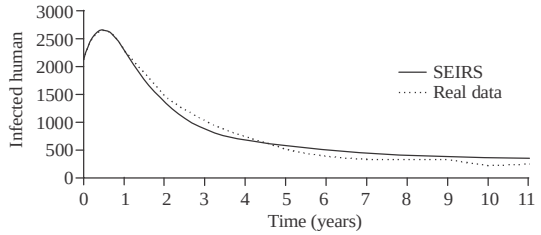

Fig. 3: Comparing the infected human produced by the model (1) with the real data

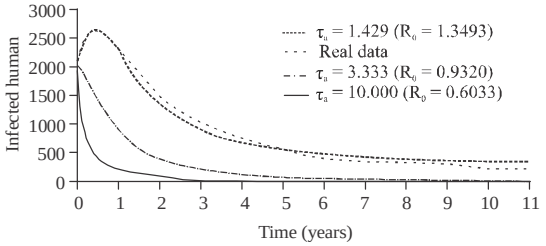

Fig. 4: Comparing the infected human produced by the model (1) with the real data as τ_a = 1.429, 3.333 and 10

number of infected human produced by the model (1) are closed to the real data as shown in Fig. 3. This study confirms that the solution of the model (1) can be used to study the dynamical behaviors of disease transmission. When the value of τ_c increases to τ_c = 3.333 and τ_c = 10, the reproductive number R_0 reduces R_0 = 0.9320 and R_0 = 0.6233, respectively. These study results verify that the number of infected human decreases as τ_c increases, Fig. 4.

As described above, it can be concluded that reducing the biting rate of mosquito leads to reduce transmission of lymphatic filariasis and other mosquito-borne infections. These study, therefore, suggest that the officer involving lymphatic filariasis control should be concern the e ective of vector control and treatment by providing enough mass drug administration to asymptomatic patient including to the entire at-risk population.

CONCLUSION

In this study, an deterministic model for the transmission dynamics of lymphatic filariasis is formulated and rigorously analyzed to gain insights into its dynamical features. The main ndings of this study are as follows.

The threshold condition called the reproduction number R_0 is derived by the next generation method. By means of Lyapunov function and LaSalles invariant set theorem, the disease-free equilibrium of the model is globally asymptotically stable whenever $R_0 \leq 1$. If $R_0 > 1$, the endemic equilibrium exists and is globally asymptotically stable whenever 0>1. Numerical simulations, using model parameter values relevant to the transmission dynamics of lymphatic filariasis are carried out to identify the relative importance of model parameters to disease transmission and prevalence.

From epidemiological point of view, if the control measures can be selected making $R_0 \leq 1$, then the disease will be eradicated from the community. The disease will persist in the community whenever the reproduction number exceeds unity. The study results also suggest that the officer involving lymphatic filariasis control should be concern the effective of vector control and treatment of asymptomatic patient would achieve filariasis control.

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