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Global Stability Analysis of Malaria Model with Prophylactic Treatment

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Abstract: In this paper, we present a mathematical model of the interaction between the human population and the vector (mosquito) population to study the stability of a malaria model in the presence of prophylactic treatment. This study is aimed at investigating the effect of the prophylactic treatment and the long-term dynamics of the solutions of the model. The graph-theoretic method was used to obtain the basic reproduction number (R_0). We obtained the disease-free equilibrium for the model which is locally and globally asymptotically stable when the basic reproduction number is less than unity. Moreover, we showed that there exists a unique endemic equilibrium whenever $R_0 > 1$, and the Lyapunov function was used to establish that the endemic equilibrium is globally asymptotically stable whenever $R_0 > 1$. The simulations show the impact of prophylactic treatment on the population of infectious individuals and the findings of this study suggest that prophylactic treatment is an effective approach to reduce the transmission of malaria as prophylactic treatment reduces the population of infectious individuals. Further numerical simulations carried out conformed with the analytic results.

Keywords: malaria, prophylactic treatment, basic reproduction number, graph-theoretic method, global stability, Lyapunov function

1. INTRODUCTION

Malaria is one of the most serious public health problems in the world. In many developing countries, it is one of the main causes of death and disease [6]. Globally, 247 million cases of malaria were recorded in 2021 and malaria claimed the lives of 619,000 people [46]. In 2020, malaria cases stood at 241 million cases globally, and an estimate of 627,000 deaths was also recorded with the WHO Africa region having the larger share of the global malaria burden [44].

Malaria is a fatal disease and one of the main causes of death for children under five years of age. It is caused by a parasite called *Plasmodium* which is transmitted through the bite of an infected female *Anopheles* mosquito. The parasite requires two hosts for the completion of its life cycle: namely, a female *Anopheles* mosquito and a human [29].

The presence of malaria depends on the climatic factors of an area, such as rainfall, humidity, and temperature, and this can be linked to the prevalence of malaria in tropical and subtropical areas where the conditions allow mosquitoes to survive, multiply, and complete their life cycle [7]. When parasites enter the human body through the bites of infected mosquitoes, the symptoms manifest themselves after about 10 to 15 days,

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and children under the age of five, pregnant women, non-immune travellers, HIV/AIDS patients and people with low immune systems are more likely to develop the disease [45]. If one is exposed to the disease, it can cause morbidity and fatality if not treated in time.

In recent times, the modelling of the transmission of infectious diseases is now influencing the theory and practice of disease management and control. Mathematical modelling now plays an important role in policy decision-making regarding the epidemiology of disease in many countries [21]. Mathematical models have become useful tools for analysing and controlling the transmission of infectious diseases, and they are used to compare, plan, implement, evaluate and optimize different detection, prevention, and control programs [16]. Several models have been formulated to explain and show the interaction between the host and vector, its transmission and control (see [1, 3, 4, 8–10, 17, 19, 26, 37, 38, 40, 42]).

Massad et al. [30] studied the malaria infection risk for travellers visiting the Amazonian region of Brazil using a mathematical modelling approach. The study reveals that the risk is high, heterogeneous and depends on the length of stay, arrival time to a locality, entomological potential, and force of infection for the population of the local vector. Mohammed-Awel and Gumel [31] worked on the mathematics of an epidemiology-genetic model to assess the effect of insecticide resistance on the dynamics of malaria transmission. The epidemiology model of the disease is coupled with the genetics of the vector population and incorporates various fitness costs associated with the insecticide resistance for the malaria model. The results of their simulations show that the Insecticides Treated Nets and Indoors Residual Spraying (ITNs & IRS) control strategies reduce the disease effectively in both moderate and high malaria transmission communities if the ITNs coverage level is high enough, but fail to manage insecticide resistance effectively in the community. Woldegerima et al. [43] studied the mathematical analysis of transmission-blocking drugs' impact on the population dynamics of malaria. Rehman et al. [35] proposed and analysed a mathematical model of malaria with multiple compartments with an associated learning mechanism between the vector-to-host and vice-versa incorporating memory, reinfection, and relapse. Traoré et al. [39] presented a mathematical model of malaria transmission with four different metamorphic stages of mosquitoes and the model also features seasonality.

Collins and Duffy [11] studied the mathematical model for the dynamics of malaria and its control in Nigeria. Epidemiological features such as drug resistance, mosquito nets use and malaria treatment were introduced into the model. The results show that the disease will remain in the country if good control measures are not geared toward dominant resistant strains, mosquito net use, and treatment. Kuddus and Rahman [22] developed a human-mosquito model for the dynamical transmission of malaria. The sensitivity analysis was carried out and the contact rates for the human and the mosquito were found to have the greatest influence on the prevalence of malaria. Moreover, the impacts of other features of the model like progression rate, disease-related death rate, recovery rate, and the rate of losing immunity were also examined. Olaniyi et al. [34] worked on the mathematical analysis of a social hierarchy-structured model for the transmission dynamics of malaria. The human population of the model was classified based on two social classes namely: low and high, and the optimal control analysis was also carried out. Beretta et al. [5] proposed a mathematical model for the transmission of malaria which features two-age and asymptomatic classes, and it was found that decreasing the biting rate and increasing the mortality rate of the mosquito can cause the endemic situation to fade off.

One of the important aspects of modelling in epidemiology is to examine the global property of the equilibrium, and the Lyapunov function, which serves as a basic and potent tool, has been widely used to study and establish the global stability of the equilibrium. Korobeinikov and Wake [20] presented the Lyapunov functions for the SIR,

SIRS, and SIS models to establish the global stability of the endemic states of the model. Vargas-De-Leon [41] studied the global stability of infectious disease models with relapse by constructing Lyapunov functions in providing the conditions for the stability of the models with relapse. Li et al. [25] presented an approach that is algebraic in nature to prove the global stability of a class of epidemic models and showed how the coefficients a_i can be chosen for the classical Lyapunov function $\sum_{i=1}^{n} a_i(x_i - x_i^* - x_i \ln x_i/x_i^*)$ so that the derivative of the Lyapunov function is negative definite or semidefinite. Khan et al. [18] examined the global stability of vector-host disease with variable population sizes, and numerical simulations were carried out to justify the theoretical results. Gebremestal [15] studied the global stability of the transmission of a malaria model with logistic growth, and the simulations examined how changes in the sustainable level of the vectors affect the population of humans. The study of endemic global stability is not only of importance to Mathematics but also helps in forecasting the long-term dynamics of the disease to design effective prevention and intervention strategies to combat the disease [36].

Most of the studies in the literature failed to consider the prophylactic treatment in malaria models. Hence, the novelty of this work is the focus on the exploration, using the Lyapunov function, of the global stability properties of a malaria model incorporating prophylactic treatment. Furthermore, it is assumed that a fraction of newly infected individuals with low immunity progress to the exposed class while the remaining fraction moves to the infectious class.

The paper is organized as follows: section 2 has the method of model design/formulation and model analysis, sections 3 and 4 contain the results and discussion of results, respectively, while the conclusion follows in section 5.

2. METHODS

2.1. Model design

In this subsection, we describe how the model is designed and formulated. The malaria model has two populations, namely the human population and the vector (mosquito) population. The overall human population (denoted by N_h) is subdivided into susceptible individuals (S_h), exposed individuals (E_M), infectious individuals (I_M), and those that recovered (R_M). Also, the total mosquito population (denoted by N_v) consists of three subpopulations, namely susceptible mosquitoes (S_v), exposed mosquitoes (E_v) and infectious mosquitoes (I_v). The susceptible humans are assumed to be recruited into the population at the rate π and get infected with malaria after being bitten by infected mosquitoes at the rate λ_M, which is given by $\lambda_M = \beta_M a I_v$, where β_M is the probability of transmission from mosquitos to humans provided that there is significant contact between the mosquito and the human, and a is the number of mosquito bites that one person has per unit time. The susceptible population has those who lost their immunity at the rate ϕ in the recovered class, and the population decreases due to natural death which does occur in all human subpopulations at the rate μ_h. It is assumed that a fraction ϵ of newly infected individuals with low immunity moves to the exposed class of humans E_M, while the remaining fraction moves to the infectious compartment I_M, the exposed humans progress into the infectious class at the rate κ, and the prophylactic treatment is given at the rate τ_1 to the exposed humans making them move to the recovered class. Those that are treated in the infectious class at the rate τ_2 progress to the recovered class and death due to the disease causes a reduction in the population of the infectious compartment. The recovered population diminishes as a result of loss of immunity at the rate ϕ and natural death at the rate μ_h which occurs in all human subpopulations.

The susceptible mosquitoes S_v come into the population at a constant rate (recruitment rate π_v), and they become infected after effective contact with people infected with malaria at the rate λ_v, where $\lambda_v = \beta_v b(E_M + \eta I_M)$ and $\eta \geq 1$ is the amplification parameter which accounts for the relative infectiousness of infectious individuals when compared to the exposed individuals, b is the number of humans bitten by mosquito per unit time and β_v is the transmission probability from humans to mosquitoes. The newly infected mosquitoes move to the exposed class of mosquitoes, and there is a progression from the exposed class to the infectious class of mosquitoes at the rate σ. The death of mosquitoes does occur in all compartments of mosquitoes at the rate μ_v. The schematic diagram of the model showing the interaction among the classes is depicted in figure 2.1 and table 2.1 shows the definitions of the parameters. Then, the system of equations of the model is as follows:

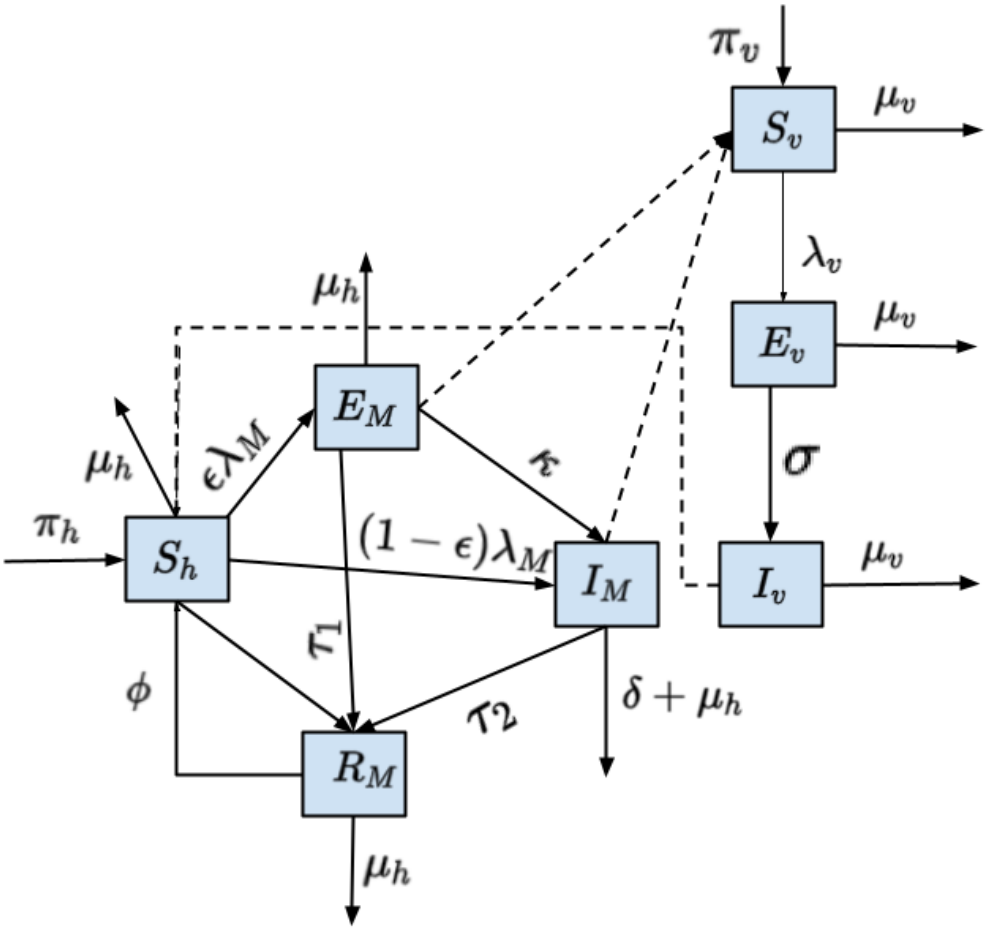

Fig. 2.1. Flow chart of the malaria model

$$\begin{aligned}
\frac{dS_h}{dt} &= \pi_h - \lambda_M S_h - \mu_h S_h + \phi R_M,\\
\frac{dE_M}{dt} &= \epsilon\lambda_M S_h - (\kappa + \tau_1 + \mu_h)E_M,\\
\frac{dI_M}{dt} &= (1-\epsilon)\lambda_M S_h + \kappa E_M - (\tau_2 + \delta + \mu_h)I_M,\\
\frac{dR_M}{dt} &= \tau_1 E_M + \tau_2 I_M - (\phi + \mu_h)R_M,\\
\frac{dS_v}{dt} &= \pi_v - \lambda_v S_v - \mu_v S_v,\\
\frac{dE_v}{dt} &= \lambda_v S_v - (\sigma + \mu_v)E_v,\\
\frac{dI_v}{dt} &= \sigma E_v - \mu_v I_v,
\end{aligned} \tag{2.1}$$

where $\lambda_M = \beta_M a I_v$, and $\lambda_v = \beta_v b(E_M + \eta I_M)$.

For convenience, we can rewrite the equations above as below:

$$\begin{aligned}
\frac{dS_h}{dt} &= \pi_h - \lambda_M S_h - \mu_h S_h + \phi R_M,\\
\frac{dE_M}{dt} &= \epsilon\lambda_M S_h - T_1 E_M,\\
\frac{dI_M}{dt} &= (1-\epsilon)\lambda_M S_h + \kappa E_M - T_2 I_M,\\
\frac{dR_M}{dt} &= \tau_1 E_M + \tau_2 I_M - T_3 R_M,\\
\frac{dS_v}{dt} &= \pi_v - \lambda_v S_v - \mu_v S_v,\\
\frac{dE_v}{dt} &= \lambda_v S_v - T_4 E_v,\\
\frac{dI_v}{dt} &= \sigma E_v - \mu_v I_v,
\end{aligned} \tag{2.2}$$

where $T_1 = \kappa + \tau_1 + \mu_h$, $T_2 = \tau_2 + \delta + \mu_h$, $T_3 = \phi + \mu_h$, and $T_4 = \sigma + \mu_v$.

2.2. Model Analysis

The analysis of the model is carried out here, and the threshold for the eradication and persistence of malaria is determined and explored.

2.2.1. The invariant region

Theorem 2.1:
The closed set

$$D = \left\{(S_h, E_M, I_M, R_M, S_v, E_v, I_v) \in R_+^7 : N_h \le \frac{\pi_h}{\mu_h}, N_v \le \frac{\pi_v}{\mu_v}\right\},$$

is positively invariant with non-negative initial values in R_+^7.

Table 2.1. Description of parameters used in the model (2.1)

Parameter	Description	Value	Source
π_h	Recruitment rate of humans	0.3913	[3]
β_M	Probability of transmission from mosquitoes to humans	0.001	[24]
μ_h	Natural death rate of humans	0.00003913	[3]
a	Number of mosquito bites per unit time	0.29	[17]
ϕ	Rate of loss of immunity	0.25	[3]
ϵ	Fraction of newly infected people with low immunity	0.6	Assumed
τ_1	Prophylactic treatment for the exposed class	0.002	Assumed
κ	Progression rate of humans from exposed to infectious class	0.0714	[32]
b	Number of humans bitten by mosquitos per unit time	0.2980	[4]
η	Amplification factor	2.5	Assumed
δ	Death due to the disease	0.00009	[8]
τ_2	Treatment rate for the infectious	0.0092	[33]
μ_v	Natural death rate of mosquitoes	0.0476	[3]
π_v	Recruitment rate of mosquitoes	0.7	Assumed
σ	Progression rate of exposed mosquitoes	0.0555	[24]
β_v	Probability of transmission from humans to mosquitos	0.0001	[24]

Proof
Consider the feasible region $D = D_h \times D_v \subset R_+^7$ with

$$D_h = \left\{ (S_h, E_M, I_M, R_M) \in R_+^4 : N_h \leq \frac{\pi_h}{\mu_h} \right\},$$

and

$$D_v = \left\{ (S_v, E_v, I_v) \in R_+^3 : N_v \leq \frac{\pi_v}{\mu_v} \right\},$$

and by adding the human and mosquito compartments of (2.1) separately with $\delta = 0$ we have

$$\frac{dN_h}{dt} = \pi_h - \mu_h N_h \text{ and } \frac{dN_v}{dt} = \pi_v - \mu_v N_v.$$

It follows that

$$\frac{dN_h}{dt} \leq \pi_h - \mu_h N_h \text{ and } \frac{dN_v}{dt} \leq \pi_v - \mu_v N_v.$$

Then

$$N_h(t) \leq N_h(0)e^{-\mu_h t} + \frac{\pi_h}{\mu_h}(1 - e^{-\mu_h t})$$

and

$$N_v(t) \leq N_v(0)e^{-\mu_v t} + \frac{\pi_v}{\mu_v}(1 - e^{-\mu_v t}).$$

If $N_h(0) \leq \frac{\pi_h}{\mu_h}$, then $N_h(t) \leq \frac{\pi_h}{\mu_h}$. Also, $N_v(0) \leq \frac{\pi_v}{\mu_v}$, then $N_v(t) \leq \frac{\pi_v}{\mu_v}$. Hence, all solutions of the model with initial values in D stay there for $t > 0$. This means that D is positively invariant and in this region, and the model is considered to be epidemiologically meaningful and mathematically well-posed. □

2.2.2. Disease-free equilibrium

The disease-free equilibrium of equation (2.2) is obtained by setting all the rates of change to zero. Hence, the disease-free equilibrium is given by

$$E_1 = (S_h, E_M, I_M, R_M, S_v, E_v, I_v) = \left(\frac{\pi_h}{\mu_h}, 0, 0, 0, \frac{\pi_v}{\mu_v}, 0, 0\right). \tag{2.3}$$

2.2.3. Basic reproduction number

We use the graph-theoretic method as given by de-Camino-Beck et al. [13] to obtain the basic reproduction number of the model. The digraph reduction procedure of the digraph $F\lambda^{-1} - V$ for the model at disease-free is shown in figure 2.2.

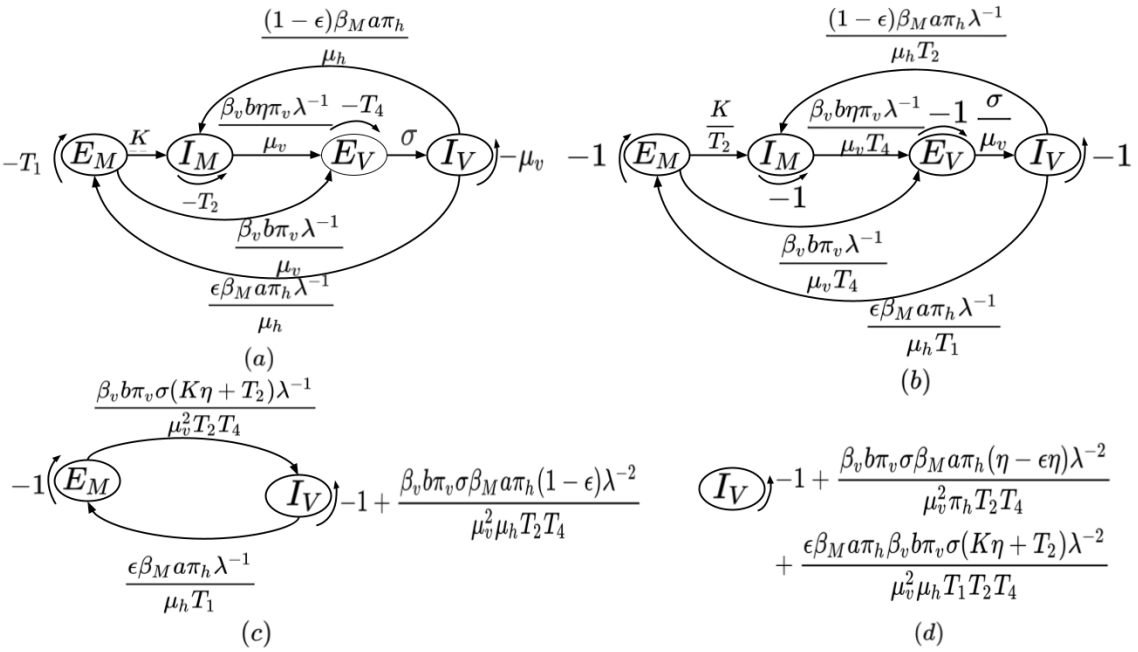

Fig. 2.2. Digraph reduction procedure of the model

From Figure 2d,

$$-1 + \frac{\beta_v b\pi_v\sigma\beta_M a\pi_h(\eta-\epsilon\eta)\lambda^{-2}}{\mu_v^2\mu_h T_2 T_4} + \frac{\epsilon\beta_M a\pi_h\beta_v b\pi_v\sigma(\kappa\eta+T_2)\lambda^{-2}}{\mu_v^2\mu_h T_1 T_2 T_4} = 0,$$

$$\therefore R_0 = \lambda = \sqrt{\frac{\beta_v b\pi_v\sigma\beta_M a\pi_h(T_1\eta - T_1\epsilon\eta + \epsilon\kappa\eta + \epsilon T_2)}{\mu_v^2\mu_h T_1 T_2 T_4}}. \tag{2.4}$$

The threshold R_0 is the basic reproduction number, which is the average number of new infection cases emanating from a single infection source when introduced in a population consisting of only susceptibles [14]. This threshold determines whether malaria will die out or persist. In the next subsection, we try to show that a small influx of infected

mosquitoes/infectious individuals into the community/environment will not generate a substantial malaria outbreak when $R_0 < 1$.

2.2.4. Local stability of the disease-free equilibrium

Theorem 2.2:
The disease-free equilibrium of the system (2.2) *given by* (2.3) *is locally asymptotically stable if* $R_0 < 1$ *and unstable when* $R_0 > 1$.

Proof
The Jacobian matrix $J(E_1)$ of the system (2.2) evaluated at disease-free equilibrium (2.3) is as given below:

$$J(E_1) = \begin{pmatrix} -\mu_h & 0 & 0 & \phi & 0 & 0 & \frac{-\beta_M a\pi_h}{\mu_h} \\ 0 & -T_1 & 0 & 0 & 0 & 0 & \frac{\epsilon\beta_M a\pi_h}{\mu_h} \\ 0 & \kappa & -T_2 & 0 & 0 & 0 & \frac{(1-\epsilon)\beta_M a\pi_h}{\mu_h} \\ 0 & \tau_1 & \tau_2 & -T_3 & 0 & 0 & 0 \\ 0 & \frac{-\beta_v b\pi_v}{\mu_v} & \frac{-\beta_v b\eta\pi_v}{\mu_v} & 0 & -\mu_v & 0 & 0 \\ 0 & \frac{\beta_v b\pi_v}{\mu_v} & \frac{\beta_v b\eta\pi_v}{\mu_v} & 0 & 0 & -T_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & \phi & -\mu_v \end{pmatrix}. \tag{2.5}$$

The first three eigenvalues of (2.5) are $-\mu_h$, $-T_3$, and $-\mu_v$. The remaining submatrix is given by

$$J(E_1) = \begin{pmatrix} -T_1 & 0 & 0 & \frac{\epsilon\beta_M a\pi_h}{\mu_h} \\ \kappa & -T_2 & 0 & \frac{(1-\epsilon)\beta_M a\pi_h}{\mu_h} \\ \frac{\beta_v b\pi_v}{\mu_v} & \frac{\beta_v b\eta\pi_v}{\mu_v} & -T_4 & 0 \\ 0 & 0 & \sigma & -\mu_v \end{pmatrix}. \tag{2.6}$$

The characteristic polynomial of the matrix (2.6) is given by

$$X_4\lambda^4 + X_3\lambda^3 + X_2\lambda^2 + X_1\lambda + X_0 = 0. \tag{2.7}$$

Where $X_4 = 1$, $X_3 = \mu_v + T_4 + T_2 + T_1$,

$$X_2 = T_1T_2 + T_1T_4 + T_1\mu_v + T_2T_4 + T_2\mu_v + T_4\mu_v,$$

$$X_1 = T_2T_4\mu_v + T_1T_4\mu_v + T_1T_2\mu_v + T_1T_2T_4\left[1 - \frac{R_0^2\mu_v\left(\eta(1-\epsilon)+\epsilon\right)}{\left[\epsilon(\eta\kappa + T_2) + T_1\eta(1-\epsilon)\right]}\right],$$

and $X_0 = T_1T_2T_4\mu_v(1 - R_0^2)$.

The characteristic equation (2.7) has negative roots if it satisfies Routh-Hurwitz criteria, such that $X_i > 0$ for $i = 0, 1, 2, 3, 4$ and $X_1(X_2X_3 - X_1) > X_0X_3^2$. Clearly, X_4, X_3 and $X_2 > 0$, $X_1 > 0$ if $\epsilon(\eta\kappa + T_2) + T_1\eta(1-\epsilon) > \mu_v(\eta(1-\epsilon)+\eta)$ and $X_0 > 0$ for $R_0 < 1$. Hence, the disease-free equilibrium is locally asymptotically stable whenever $R_0 < 1$. □

This theorem 2.2 implies that there is possibility of malaria eradication (when $R_0 < 1$) if the initial subpopulation sizes are in the basin of attraction of the disease-free equilibrium E_1. To ensure that malaria eradication is not dependent on the initial subpopulations sizes, it is vital to show that the disease-free equilibrium of malaria is globally asymptotically stable.

2.2.5. Global stability of disease-free equilibrium

Theorem 2.3:
The disease-free equilibrium given by (2.3) *is globally asymptotically stable when* $R_0 < 1$.

Proof
We construct the Lyapunov function to prove the global stability of the disease-free as thus:

$$L = (\kappa\eta + T_2)E_M + T_1\eta I_M + \frac{T_2T_1R_0}{\beta_v bS_v}E_v + \frac{T_4T_2T_1R_0}{\sigma\beta_v bS_v}I_v. \tag{2.8}$$

Differentiating equation (2.8) gives

$$\dot{L} = (\kappa\eta + T_2)\dot{E_M} + T_1\eta\dot{I_M} + \frac{T_2T_1R_0}{\beta_v bS_v}\dot{E_v} + \frac{T_4T_2T_1R_0}{\sigma\beta_v bS_v}\dot{I_v}. \tag{2.9}$$

$$\begin{aligned}\dot{L} &= (\kappa\eta + T_2)[\epsilon\beta_M aI_vS_v - T_1E_M] + T_1\eta[(1-\epsilon)\beta_M aI_vS_h + \kappa E_M - T_2I_M] \\ &\quad + \frac{T_2T_1R_0}{\beta_v bS_v}[\beta_v b(E_M + \eta I_M)S_v - T_4E_v] + \frac{T_4T_2T_1R_0}{\sigma\beta_v bS_v}[\sigma E_v - \mu_v I_v].\end{aligned}$$

$$\begin{aligned}\dot{L} &= \frac{\kappa\eta\epsilon\beta_M aI_v\pi_h}{\mu_h} + \frac{T_2\epsilon\beta_M aI_v\pi_h}{\mu_h} - T_1T_2E_M + \frac{T_1\eta(1-\epsilon)\beta_M aI_v\pi_h}{\mu_h} \\ &\quad - T_1\eta T_2I_M + T_2T_1R_0E_M + T_2T_1\eta R_0I_M - \frac{T_4T_2T_1R_0I_v\mu_v^2}{\sigma\beta_v b\pi_v}.\end{aligned}$$

$$\dot{L} = \left[\sqrt{\frac{T_1T_2T_4\beta_M a\pi_h\mu_v^2}{\sigma\beta_v b\pi_v\mu_h}}I_v + T_1T_2E_M + T_1T_2\eta I_M\right]R_0 - 1. \tag{2.10}$$

Therefore, $\dot{L} < 0$ if $R_0 < 1$ with $\dot{L} = 0$ if and only if $E_M = I_M = I_v = 0$. Also, the largest invariant set in $\{(S_h, E_M, I_M, R_M, S_v, E_v, I_v) \in D : \dot{L} = 0\}$ is the singleton E_1. By the LaSalle Invariance Principle [23], every solution that starts in D approaches E_1 as $t \to \infty$. Therefore, the disease-free equilibrium is globally asymptotically stable whenever $R_0 < 1$. □

The implication of theorem 2.3 epidemiologically is that malaria can be eradicated regardless of the initial sizes of the subpopulations of the model whenever the basic reproduction number is less than unity.

2.2.6. Existence of endemic equilibrium
The condition for which the endemic equilibrium exists is investigated here. Let

$$E_2^* = (S_h^*, E_M^*, I_M^*, R_M^*, S_v^*, E_v^*, I_v^*),$$

represents an arbitrary endemic equilibrium of the system of equations (2.2). Also, let λ_M and λ_v at endemic steady state be denoted by λ_M^* and λ_v^* and given by

$$\lambda_M^* = \beta_M aI_v^*, \tag{2.11}$$

$$\lambda_v^* = \beta_v b(E_M^* + \eta I_M^*). \tag{2.12}$$

When we solve the equations of model (2.2) at steady state in terms of the forces of infection λ_M^* and λ_v^* , we will have

$$S_h^* = \frac{\pi_h}{\mu_h + \lambda_M^*(1-\phi P_3)},\ E_M^* = P_1\lambda_M^* S_h^*, \quad I_M^* = P_2\lambda_M^* S_h^*,\ R_M^* = P_3\lambda_M^* S_h^*, \quad (2.13)$$

$$S_v^* = \frac{\pi_v}{\lambda_v^* + \mu_v},\ E_v^* = P_4\lambda_v^* S_v^*, \qquad I_v^* = P_5\lambda_v^* S_v^*. \quad (2.14)$$

where

$$P_1 = \frac{\epsilon}{T_1}, \qquad P_2 = \frac{(1-\epsilon)T_1 + \kappa\epsilon}{T_1T_2}, \qquad P_3 = \frac{T_2\tau_1\epsilon + \tau_2((1-\epsilon)T_1 + \kappa\epsilon)}{T_1T_2T_3},$$
$$P_4 = \frac{1}{T_4}, \qquad P_5 = \frac{\sigma}{\mu_v T_4}.$$

and T_1, T_2, T_3, T_4, and T_5 are defined in (2.2) above. By substitution of (2.13) and (2.14) into (2.11) and (2.12), we have

$$\lambda_M^* = \beta_M a P_5 \lambda_v^* S_v^*, \quad (2.15)$$

$$\lambda_v^* = \beta_v b(P_1\lambda_M^* S_h^* + \eta P_2\lambda_M^* S_h^*). \quad (2.16)$$

Further substitution leads to

$$c\lambda_M^* - d = 0,$$

where $d = \mu_v\mu_h({R_0}^2 - 1)$ and $c = \beta_v b\pi_h(P_1 + \eta P_2) + \mu_v(1 - \phi P_3)$. Then

$$\lambda_M^* = \frac{d}{c}. \quad (2.17)$$

From (2.17), it shows clearly that $c > 0$ and $d > 0$ if $R_0 > 1$. Then, λ_M is positive (greater than zero) whenever $R_0 > 1$. Hence, the following result is established:

Lemma 2.1:
There exists a unique endemic equilibrium for the model if the basic reproduction number $R_0 > 1$.

2.2.7. Global stability of endemic equilibrium
The global stability of the endemic equilibrium of the model is considered here for the case when $\phi = 0$, and we take $\epsilon = 1$.

Theorem 2.4:
The unique endemic equilibrium of the model with $\phi = 0$ *and* $\epsilon = 1$ *is globally asymptotically stable whenever* $R_{0_{|\phi=0,\epsilon=1}} > 1$.

Proof
The Volterra type of Lyapunov function stated in 2.18 is used to prove the global stability of the endemic equilibrium.

$$\begin{aligned} L &= \left(S_h - S_h^* ln\frac{S_h}{S_h^*}\right) + \left(E_M - E_M^* ln\frac{E_M}{E_M^*}\right) + \frac{T_1}{\kappa}\left(I_M - I_M^* ln\frac{I_M}{I_M^*}\right) \\ &+ \left(S_v - S_v^* ln\frac{S_v}{S_v^*}\right) + \left(E_v - E_v^* ln\frac{E_v}{E_v^*}\right) + \frac{T_4}{\sigma}\left(I_v - I_v^* ln\frac{I_v}{I_v^*}\right). \end{aligned} \quad (2.18)$$

Taking the derivative of (2.18), we have

$$\begin{aligned}\dot{L} &= \dot{S}_h - \frac{S_h^*}{S_h}\dot{S}_h + \dot{E_M} - \frac{E_M^*}{E_M}\dot{E_M} + \frac{T_1}{\kappa}\left(\dot{I_M} - \frac{I_M^*}{I_M}\dot{I_M}\right) + \dot{S}_v - \frac{S_v^*}{S_v}\dot{S}_v \\ &+ \dot{E}_v - \frac{E_v^*}{E_v}\dot{E}_v + \frac{T_4}{\sigma}\left(\dot{I_M} - \frac{I_M^*}{I_M}\dot{I_M}\right). \end{aligned} \tag{2.19}$$

$$\begin{aligned}\dot{L} &= 2\lambda_M S_h^* + 2\mu_h S_h^* - \mu_h S_h - \frac{\lambda_M S_h^{*2}}{S_h} - \frac{\mu_h S_h^{*2}}{S_h} - \frac{\lambda_M S_h E_M^*}{E_M} + T_1 E_M^* \\ &- \frac{T_1 E_M^* I_M}{I_M} - \frac{T_1 E_M I_M^*}{I_M} + T_1 E_M + 2\lambda_v S_v^* + 2\mu_v S_v^* - \mu_v S_v - \frac{\lambda_v S_v^{*2}}{S_v} \\ &- \frac{\mu_v S_v^{*2}}{S_v} - \frac{\lambda_v S_v E_M^*}{E_v} + T_4 E_v^* - \frac{T_4 E_M^* I_v}{I_v^*} - \frac{T_4 E_v I_v^*}{I_v} + T_4 E_v^*. \end{aligned}$$

$$\begin{aligned}\dot{L} &= T_1 E_M^*\left(2 - \frac{S_h^*}{S_h}\right) + \mu_h S_h^*\left(2 - \frac{S_h^*}{S_h}\right) - \mu_h S_h - \frac{T_1 E_M^{*2} S_h}{S_h^* E_M} + T_1 E_M^* \\ &- \frac{T_1 E_M^* I_M}{I_M^*} - \frac{T_1 E_M I_M^*}{I_M} + T_1 E_M^* + T_4 S_v^*\left(2 - \frac{S_v^*}{S_v}\right) + \mu_v S_v^*\left(2 - \frac{S_v^*}{S_v}\right) \\ &- \mu_v S_v - \frac{T_4 E_v^{*2} S_v}{S_v E_v} + T_4 E_v^* - \frac{T_4 E_v^* I_v}{I_v^*} - \frac{T_4 E_v I_v^*}{I_v} + T_4 E_v^*. \end{aligned} \tag{2.20}$$

By simplification, (2.20) becomes

$$\begin{aligned}\dot{L} &= \mu_h S_h^*\left(2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*}\right) + T_1 E_M^*\left(4 - \frac{S_h^*}{S_h} - \frac{E_M^* S_h^*}{E_M S_h^*} - \frac{E_M I_M^*}{E_M^* I_M} - \frac{I_M}{I_M^*}\right) \\ &+ \mu_v S_v^*\left(2 - \frac{S_v^*}{S_v} - \frac{S_v}{S_v^*}\right) + T_4 E_v^*\left(4 - \frac{S_v^*}{S_v} - \frac{E_v^* S_v}{E_v S_v^*} - \frac{I_v}{I_v^*} - \frac{E_v I_v^*}{E_v^* I_v}\right). \end{aligned} \tag{2.21}$$

Since the arithmetic mean is greater than the geometric mean, then

$$2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*} \le 0, \qquad 4 - \frac{S_h^*}{S_h} - \frac{E_M^* S_h^*}{E_M S_h^*} - \frac{E_M I_M^*}{E_M^* I_M} - \frac{I_M}{I_M^*} \le 0,$$
$$2 - \frac{S_v^*}{S_v} - \frac{S_v}{S_v^*} \le 0, \qquad 4 - \frac{S_v^*}{S_v} - \frac{E_v^* S_v}{E_v S_v^*} - \frac{I_v}{I_v^*} - \frac{E_v I_v^*}{E_v^* I_v} \le 0.$$

With all the parameters of the model being positive, therefore, $\dot{L} \le 0$ for $R_{0_{|\phi=0,\epsilon=1}} > 1$. Hence, by the LaSalle Invariance Principle [23], every solution to the model equations approaches the endemic equilibrium E_2 as $t \to \infty$ whenever $R_{0_{|\phi=0,\epsilon=1}} > 1$. □

The epidemiological implication of theorem 2.4 is that malaria will persist in the community irrespective of the initial sizes of the populations of the model whenever $R_0 > 1$.

3. RESULTS

The results of the numerical simulations of the model are obtained using the ODE45 solver of MatLab and the values of the parameters used for the simulations are given in

table 2.1. We investigate the influence of prophylaxis on the dynamics of malaria and the long-term dynamics of the model. The results of the simulations are depicted in figures 3.3 - 3.6.

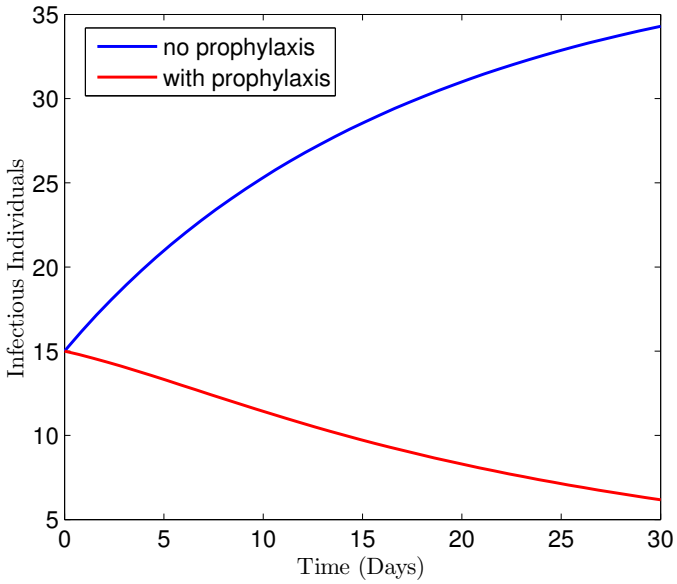

Fig. 3.3. Graph of the effect of the prophylactic treatment on the infectious population

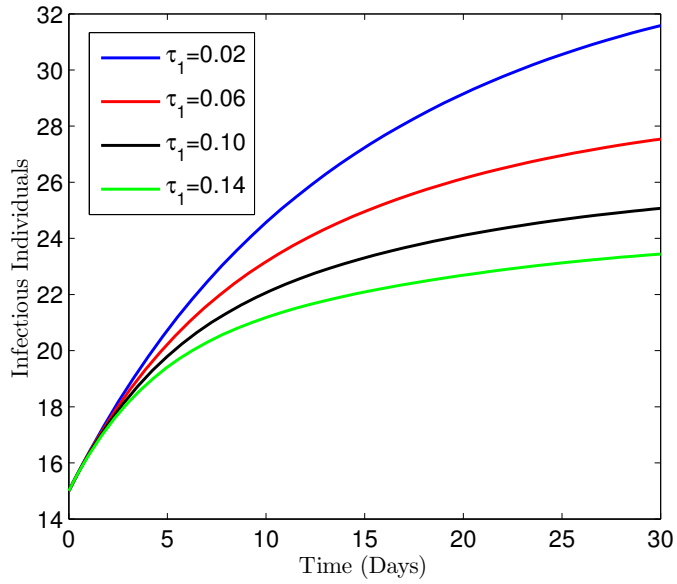

Fig. 3.4. Graph of the infectious population at different values of prophylactic treatment rate (τ_1)

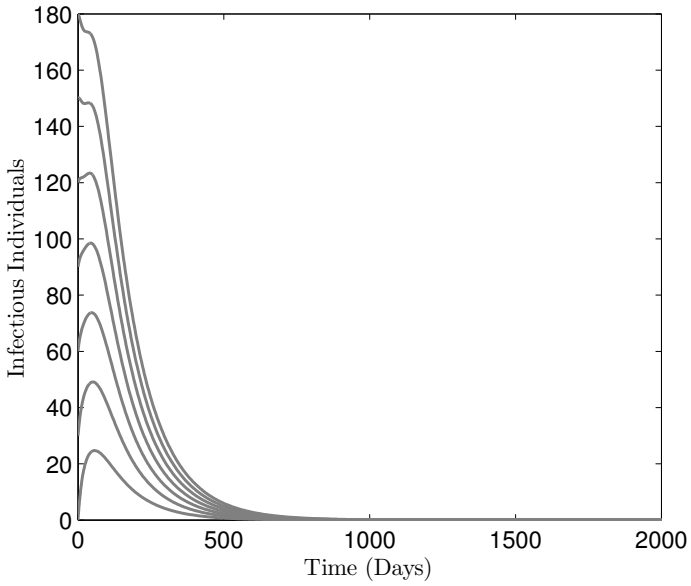

Fig. 3.5. Plot of the infectious individuals at different initial conditions when $R_0 = 0.65$ and the parameters used are given in Table 2.1

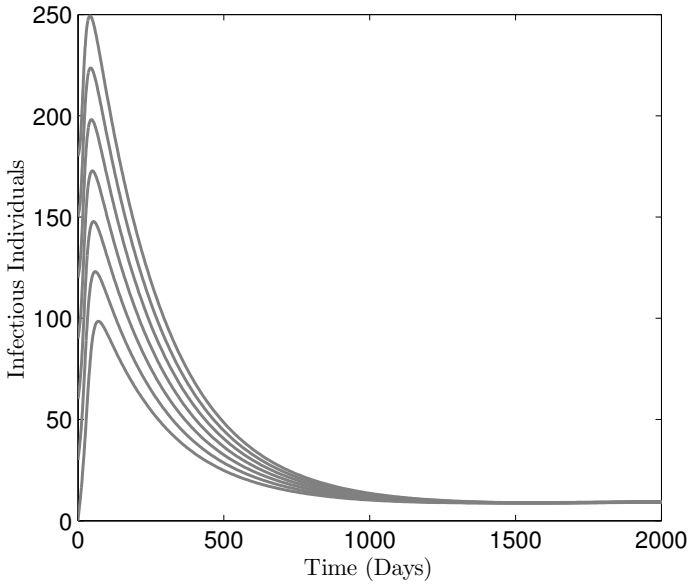

Fig. 3.6. Plot of the infectious individuals at different initial conditions when $R_0 = 12.4$, with $\epsilon = 1$, $\phi = \delta = 0$, $\beta_M = 0.004$, $\beta_v = 0.0004$, $\tau_1 = 0.001$, $\tau_2 = 0.004$, $\mu_v = 0.0175$ and other parameters used are given in Table 2.1

4. DISCUSSION OF THE RESULTS

A mathematical model of malaria with prophylactic treatment is presented, and its global asymptotic stability properties are studied. The threshold which determines whether malaria will fade out or persist is established. The qualitative analysis of the stability carried out showed that the disease-free equilibrium is locally asymptotically

stable whenever $R_0 < 1$. Also, there exists an endemic equilibrium whenever the basic reproduction number goes beyond unity. The Lyapunov functions were used to establish that the disease-free equilibrium and endemic equilibrium are globally asymptotically stable whenever $R_0 < 1$ and $R_0 > 1$, respectively. The graph of figure 3.3 illustrates the population of infectious individuals when prophylactic treatment is present and when there is no prophylactic treatment. The population of infectious individuals is at minimum when there is prophylaxis as compared to when there is none. Hence, the presence of prophylactic treatment lowers the number of infectious individuals as it prevents exposed individuals to progress to the infectious class/state. The increasing effect of prophylactic treatment rate on the infectious population is depicted in figure 3.4. The population of infectious individuals diminishes as the prophylactic treatment rate increases and thereby reducing the burden of the disease. Therefore, prophylactic treatment plays an important role in reducing the population of the infectious individuals. The practical situation of the study is the recent implementation of seasonal malaria chemoprophylaxis in Nigeria by the Malaria Consortium [27, 28] to reduce the disease burden. Some states in Nigeria were selected for the pilot phase and every child in the community under five years old is given prophylactic treatment every month. A study by de Cola et al. [12] reported that the treatment programme reduces the prevalence of malaria in the country, which is in line with the result of this current study. The work of Ambe et al. [2] also supports the result we obtained. We carried out numerical simulations on global stability to validate the analytic results. The plot in Fig. 3.5 shows the long-term dynamics of the population of infectious individuals at different initial conditions when $R_0 < 1$. The infectious population converges to disease-free equilibrium and vanishes, which means that the disease dies out of the community irrespective of the different initial sizes of the infectious class. Also, Fig. 3.6 shows a scenario of the population of the infectious class with different initial conditions when the basic reproduction number $R_0 > 1$. In this case, the disease does clear out from the population, but persists, and this is in line with the analytic result.

5. CONCLUSION

We formulated a mathematical model for the dynamics of malaria with prophylaxis to study the global stability properties of the model. The basic reproduction number was obtained using the graph-theoretic method. The disease-free equilibrium is proved to be locally and globally asymptotically stable whenever the basic reproduction number is less than unity. We showed that there exists a unique endemic equilibrium whenever the basic reproduction number surpasses unity, and by the Lyapunov function, the endemic equilibrium is globally asymptotically stable whenever $R_0 > 1$. The presence of prophylaxis plays a vital role as it minimizes the population of infectious individuals and mitigates the burden of malaria. Hence, there is a need to intensify efforts in the provision of good and appropriate prophylaxis to reduce the burden of the disease. Further numerical simulations carried out justified the analytic results.

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