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Global Stability and Sensitivity Analysis of Basic Reproduction Number of a Malaria Model

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Abstract: This paper explores a mathematical model of malaria, focusing on the basic reproduction number ($\mathcal{R}_0$) and employing Lyapunov functions to assess the global stability of disease-free and endemic equilibria. Sensitivity analysis of key parameters is conducted to evaluate their impact on disease control. The results indicate an active malaria outbreak with decreasing human classes signifying disease progression and increasing mosquito classes suggesting heightened transmission risk. Effective control measures, including mosquito control and treatment of infected individuals, are essential to mitigate the outbreak.

Keywords: malaria, sensitivity, global stability analysis, numerical simulations, Lyaponov function

1. INTRODUCTION

Malaria is a life threatening tropical disease. It is both preventable and treatable. A case of simple malaria, however, can escalate to a severe form of the disease, which is generally fatal if not treated promptly. This risk of infection is higher in some locations than others, depending on a variety of circumstances, including the species of local mosquitoes. It may also vary according to season, with the danger being greatest in tropical nations during the rainy season [6, 17].

The risk of disease can be lowered by preventing mosquito bites with mosquito nets and insect repellents, or by using mosquito-control techniques such as spraying insecticides. Malaria is still frequent in tropical and subtropical nations, despite the fact that it is uncommon in temperate climes. Globally, the World Health Organization estimates that 241 million clinical cases of malaria will occur in 2020, with 627,000 deaths, the majority of whom would be children in Africa. The first signs of malaria usually appear after 10-15 days of being bitten by an infected mosquito. Fever, headache, and chills are common symptoms, however they could be minor and difficult to distinguish from malaria. In malaria-endemic settings, people who have developed partial immunity may become infected yet exhibit no symptoms [12, 13]. Over the years, precise frameworks for comprehending the dynamics of malaria transmission in the human population have been developed using mathematical

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models [3–5, 11]. The model developed by [2] ia considered in this study in order to determine the effect of the sensitive parameters to the disease control. Further studies on malaria models can be found in [2].The motivation for this study stems from the persistent threat of malaria as a life-threatening disease transmitted by mosquitoes, posing a significant public health challenge for many years. Recognizing the gravity of the issue, this research endeavors to explore a sophisticated mathematical model of malaria. By incorporating the fundamental epidemiological indicator, the basic reproduction number ($\mathcal{R}_0$), and employing Lyapunov functions, we aimed to gain insights into the global stability of disease-free and endemic equilibria. Furthermore, the study's motivation extended to conducting a sensitivity analysis of key parameters, shedding light on their influence in the context of disease control. The findings revealing an active malaria outbreak, characterized by diminishing human populations and burgeoning mosquito populations, underscore the urgency for effective control measures. Ultimately, the study's motivation lies in the imperative need to address this ongoing health crisis through measures such as mosquito control and timely treatment of infected individuals, with the ultimate goal of mitigating the outbreak and safeguarding public health. The paper is structured as follows: section two deals with the models formulation, section three deals with the basic analysis of the model, section four deals with the sensitivity analysis of the model and discussion of result. Finally, we concluded the study in section five.

2. MODEL FORMULATION

This model developed is an extension of [2] by considering the global stabilities and sensitivity analysis of the model. According to [2], the total population of humans, $N_h(t)$ which is known as the host comprises of Susceptible class of human ($S_h(t)$), Exposed class of human ($E_h(t)$), Infectious class of human ($I_h(t)$) and Recovered class of human ($R_h(t)$). This can be defined as

$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + R_h(t)$$

Similarly, the total population of mosquitoes, $N_{\mathrm{v}}(t)$ which is also known as vector comprises of Susceptible class of mosquito ($S_{\mathrm{v}}(t)$), Exposed class of mosquito ($E_{\mathrm{v}}(t)$) and Infectious class of mosquito ($I_{\mathrm{v}}(t)$). This can be defined as

$$N_{\mathrm{v}}(t) = S_{\mathrm{v}}(t) + E_{\mathrm{v}}(t) + I_{\mathrm{v}}(t)$$

Moreover, the parameters of human and mosquito populations show the movement of individual at different rates from one class to another. This can be defined below as follows; Λ_h and Λ_{v} represent the recruitment rates of humans and mosquitoes respectively, σ_h and σ_{v} represent the the Probability of transmission of malaria per mosquito bite to susceptible humans and from infected humans to susceptible mosquitoes respectively. μ and η represent natural mortality rates of humans and mosquitoes respectively. Also, υ is the developing rate of exposed humans and ψ is the rate of the newborn birth with malaria from the mother's womb. ε_h and ε_{v} represent the proportion of an antibody produced by human in response to the incidence of infection caused by mosquito and produced by mosquito in response to the incidence of infection caused by human respectively. δ_h and δ_{v} represent the disease-induced mortality rates of humans and mosquitoes respectively. ξ is the biting rate of mosquitoes and α is the developing rate of exposed mosquitoes. γ_1 and γ_2 represent the rate of loss of immunity in humans and relapse rate of humans respectively. ω is the recovery rate of of humans.

2.1. Flow Chart of the Model

The diagram below is the flow chart of the model.

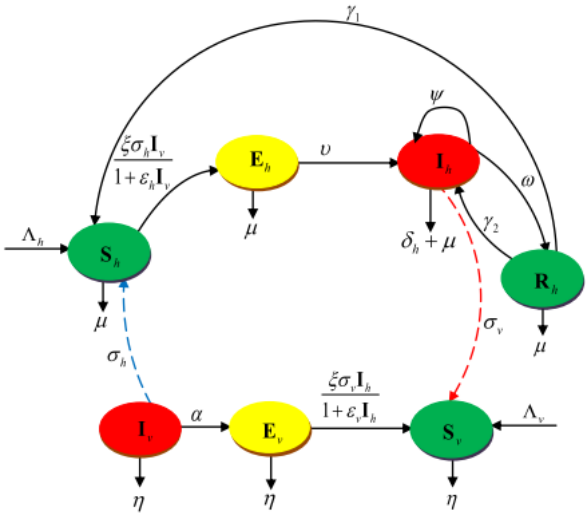


Fig. 2.1. Flow chart diagram

2.2. Differential Equations of the Model

The first order differential equations can be derived from the flow chart model as follows:

$$\begin{aligned}
\frac{dS_h}{dt} =& \Lambda_h - \frac{\xi\sigma_h I_{\mathrm{v}} S_h}{1+\epsilon_h I_{\mathrm{v}}} - \mu S_h + \gamma_1 R_h \\
\frac{dE_h}{dt} =& \frac{\xi\sigma_h I_{\mathrm{v}} S_h}{1+\epsilon_h I_{\mathrm{v}}} - (\upsilon+\mu) E_h \\
\frac{dI_h}{dt} =& \upsilon E_h - (\omega+\mu+\delta_h) I_h + \psi I_h + \gamma_2 R_h \\
\frac{dR_h}{dt} =& \omega I_h - (\gamma_1+\gamma_2+\mu)\, R_h \\
\frac{dS_{\mathrm{v}}}{dt} =& \Lambda_{\mathrm{v}} - \frac{\xi\sigma_{\mathrm{v}} I_h S_{\mathrm{v}}}{1+\epsilon_{\mathrm{v}} I_h} - \eta S_{\mathrm{v}} \\
\frac{dE_{\mathrm{v}}}{dt} =& \frac{\xi\sigma_{\mathrm{v}} I_h S_{\mathrm{v}}}{1+\epsilon_{\mathrm{v}} I_h} - (\alpha+\eta) E_{\mathrm{v}} \\
\frac{dI_{\mathrm{v}}}{dt} =& \alpha E_{\mathrm{v}} - (\eta+\delta_{\mathrm{v}}) I_{\mathrm{v}}
\end{aligned} \tag{2.1}$$

3. EXISTENCE OF EQUILIBRIUM POINTS

It is very important to study the equilibrium points of the model (2.1) which comprises of Disease Free Equilibrium (DFE) point and Endemic Equilibrium Point (EEP). Therefore, to show that the DFE exists by setting the right hand sides of each of the equations in model (2.1) to be zero and substituting $E_h = I_h = R_h = E_{\mathrm{v}} = I_{\mathrm{v}} = 0$ to obtain

$$(S_h, E_h, I_h, R_h, S_{\mathrm{v}}, E_{\mathrm{v}}, I_{\mathrm{v}}) = \left(\frac{\Lambda_h}{\mu}, 0, 0, 0, \frac{\Lambda_{\mathrm{v}}}{\eta}, 0, 0\right) \tag{3.2}$$

Also, for the endemic, setting the right hand sides of the equations in model (2.1) to be zero and substituting $S_h = S_h^*$, $E_h = E_h^*$, $I_h = I_h^*$, $R_h = R_h^*$, $S_{\mathrm{v}} = S_{\mathrm{v}}^*$, $E_{\mathrm{v}} = E_{\mathrm{v}}^*$ and $I_{\mathrm{v}} = I_{\mathrm{v}}^*$ to

obtain

$$\begin{aligned}
S_h^* =& \frac{(\Lambda_h + \gamma_1 R_h^*)(1 + \epsilon_h I_{\rm v}^*)}{\mu(1 + \epsilon_h I_{\rm v}^*) + \xi\sigma_h I_{\rm v}^*} \\
E_h^* =& \frac{\xi\sigma_h I_{\rm v}^* S_h^*}{(1 + \epsilon_h I_{\rm v}^*)(\upsilon + \mu)} \\
I_h^* =& \frac{\upsilon E_h^* + \gamma_2 R_h^*}{\omega + \mu + \delta_h - \psi} \\
R_h^* =& \frac{\omega I_h^*}{\gamma_1 + \mu + \gamma_2} \\
S_{\rm v}^* =& \frac{\Lambda_{\rm v}(1 + \epsilon_{\rm v} I_h^*)}{\eta(1 + \epsilon_{\rm v} I_h^*) + \xi\sigma_{\rm v} I_h^*} \\
E_{\rm v}^* =& \frac{\xi\sigma_{\rm v} I_h^* S_{\rm v}^*}{(1 + \epsilon_{\rm v} I_h^*)(\alpha + \eta)} \\
I_{\rm v}^* =& \frac{\alpha E_{\rm v}^*}{\eta + \delta_{\rm v}}
\end{aligned} \tag{3.3}$$

Therefore, eq. (3.2) has shown that we can have two equilibriums in the non-negative of $\mathbb{R}_+^7$ thus, the existence of Disease Free Equilibrium (DFE) point $E_0 = \left(\frac{\Lambda_h}{\mu}, 0, 0, 0, \frac{\Lambda_{\rm v}}{\eta}, 0, 0\right)$ and eq. (3.3) has shown the existence of Endemic Equilibrium point (EEP), $E_1 = (S_h^*, E_h^*, I_h^*, R_h^*, S_{\rm v}^*, E_{\rm v}^*, I_{\rm v}^*)$

3.1. Basic Reproduction Number $(\mathcal{R}_0)$

This section describes how to derive basic reproduction number $\mathcal{R}_0$ of the disease free equilibrium (DFE) using next generation matrix method. According to [18], if $\mathbf{F}$ denotes the rate of appearance of new infections and $\mathbf{V}$ denotes the rate of transfer of the DFE, then $\mathbf{FV}^{-1}$ is called "Next Generation Matrix". Therefore

$$\mathcal{F}(X) = \begin{pmatrix} \dfrac{\xi\sigma_h I_{\rm v} S_h}{1 + \epsilon_h I_{\rm v}} \\ 0 \\ \dfrac{\xi\sigma_{\rm v} I_h S_{\rm v}}{1 + \epsilon_{\rm v} I_h} \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

and

$$\mathcal{V}(X) = \begin{pmatrix} (\upsilon + \mu)E_h \\ (\omega + \mu + \delta_h - \psi)I_h - \upsilon E_h - \gamma_2 R_h \\ (\alpha + \eta)E_{\rm v} \\ (\eta + \delta_{\rm v})I_{\rm v} - \alpha E_{\rm v} \\ \mu S_h - \Lambda_h - \gamma_1 R_h \\ (\gamma_1 + \mu + \gamma_2)R_h - \psi I_h \\ \eta S_{\rm v} - \Lambda_{\rm v} \end{pmatrix}$$

Solving the above matrices using Jacobian Matrix at the disease free equilibrium, $E_0 = \left(\frac{\Lambda_h}{\mu}, 0, 0, 0, \frac{\Lambda_{\rm v}}{\mu}, 0, 0\right)$, we obtain

$$\mathbf{F} = \begin{pmatrix} 0 & 0 & 0 & \frac{\xi\sigma_h\Lambda_h}{\mu} \\ 0 & 0 & 0 & 0 \\ 0 & \frac{\xi\sigma_{\rm v}\Lambda_{\rm v}}{\eta} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$\mathbf{V} = \begin{pmatrix} \upsilon+\mu & 0 & 0 & 0 \\ -\upsilon & \omega+\mu+\delta_h-\psi & 0 & 0 \\ 0 & 0 & \alpha+\eta & 0 \\ 0 & 0 & -\alpha & \eta+\delta_{\rm v} \end{pmatrix}$$

respectively. Thus, [18] basic reproduction number $\mathcal{R}_0$ means the predominant eigenvalue equivalent to the Spectral radius of matrix $\mathbf{FV}^{-1}$. Mathematically, $\mathcal{R}_0 = \rho(\mathbf{FV}^{-1})$ where ρ is the Spectral radius. Therefore;

$$\mathcal{R}_0 = \sqrt{\frac{\upsilon\xi\sigma_h\Lambda_h}{\mu(\upsilon+\mu)(\omega+\mu+\delta_h-\psi)}\frac{\alpha\xi\sigma_{\rm v}\Lambda_{\rm v}}{\eta(\alpha+\eta)(\eta+\delta_{\rm v})}} \tag{3.4}$$

3.2. Global Stability Analysis of Disease-Free Equilibrium

Theorem 3.1:
If $\mathcal{R}_0 \leq 1$ then the disease free equilibrium E_0 given by equation (3.4) *is globally asymptotically stable. Otherwise, it is unstable.*

Proof
Let us formed Lyapunov function of the type

$$\mathfrak{L} = \frac{\upsilon E_h}{(\upsilon+\mu)(\omega+\mu+\delta_h-\psi)} + \frac{I_h}{(\omega+\mu+\delta_h-\psi)} + \frac{\eta\mathcal{R}_0 E_{\rm v}}{\xi\sigma_{\rm v}\Lambda_{\rm v}} + \frac{\eta(\alpha+\eta)\mathcal{R}_0 I_{\rm v}}{\xi\sigma_{\rm v}\alpha\Lambda_{\rm v}} \tag{3.5}$$

It is easy to identify that the coefficient of each state variables of the above eq. (3.5) are non-negative. Thus, differentiating (3.5) as well as substitution model (2.1) to obtain

$$\begin{aligned} \dot{\mathfrak{L}} =& \frac{\upsilon}{(\upsilon+\mu)(\omega+\mu+\delta_h-\psi)}\left(\frac{\xi\sigma_h I_{\rm v} S_h}{1+\epsilon_h I_{\rm v}} - (\upsilon+\mu)E_h\right) + \\ & \frac{1}{(\omega+\mu+\delta_h-\psi)}\left(\upsilon E_h - (\omega+\mu+\delta_h-\psi)I_h + \gamma_2 R_h\right) + \\ & \frac{\eta\mathcal{R}_0}{\xi\sigma_{\rm v}\Lambda_{\rm v}}\left(\frac{\xi\sigma_{\rm v} I_h S_{\rm v}}{1+\epsilon_{\rm v} I_h} - (\alpha+\eta)E_{\rm v}\right) + \frac{\eta(\alpha+\eta)\mathcal{R}_0}{\xi\sigma_{\rm v}\alpha\Lambda_{\rm v}}\left(\alpha E_{\rm v} - (\eta+\delta_{\rm v})I_{\rm v}\right) \end{aligned} \tag{3.6}$$

It is assume that if $\epsilon_h = 0$ then the saturated incidence $\left(\frac{\xi\sigma_h I_{\rm v} S_h}{1+\epsilon_h I_{\rm v}}\right)$ becomes bilinear incidence $(\xi\sigma_h I_{\rm v} S_h)$. Similarly, if $\epsilon_{\rm v} = 0$ then the saturated incidence $\left(\frac{\xi\sigma_{\rm v} I_h S_{\rm v}}{1+\epsilon_{\rm v} I_h}\right)$ becomes bilinear incidence $(\xi\sigma_{\rm v} I_h S_{\rm v})$ [4, 7, 10, 14]. Epidemiologically, it is assumed that, in humans,

the rate of antibodies produced against the antigens of human is zero (i.e. $\epsilon_h = 0$) and in mosquitoes, the rate of antibodies produced against the antigens of mosquitoes is zero (i.e. $\epsilon_{\mathrm{v}} = 0$). Thus, eq. (3.6) becomes

$$\begin{aligned}\dot{\mathfrak{L}} =& \frac{\upsilon}{(\upsilon+\mu)(\omega+\mu+\delta_{\mathrm{v}}h-\psi)}\left(\xi\sigma_h I_{\mathrm{v}} S_h - (\upsilon+\mu)E_h\right)\\ &+\frac{1}{(\omega+\mu+\delta_h-\psi)}\left(\upsilon E_h - (\omega+\mu+\delta_h-\psi)I_h+\gamma_2 R_h\right)\\ &+\frac{\eta\mathcal{R}_0}{\xi\sigma_{\mathrm{v}}\Lambda_{\mathrm{v}}}\left(\xi\sigma_{\mathrm{v}} I_h S_{\mathrm{v}} - (\alpha+\eta)E_{\mathrm{v}}\right)+\frac{\eta(\alpha+\eta)\mathcal{R}_0}{\xi\sigma_{\mathrm{v}}\alpha\Lambda_{\mathrm{v}}}\left(\alpha E_{\mathrm{v}} - (\eta+\delta_{\mathrm{v}})I_{\mathrm{v}}\right)\end{aligned}$$

$$\begin{aligned}\dot{\mathfrak{L}} =& \left(\frac{\upsilon\xi\sigma_h S_h}{(\upsilon+\mu+\delta_h)(\omega+\mu+\delta_h-\psi)} - \frac{\eta(\alpha+\eta)(\eta+\delta_{\mathrm{v}})\mathcal{R}_0}{\xi\sigma_{\mathrm{v}}\Lambda_{\mathrm{v}}\alpha}\right) I_{\mathrm{v}}\\ &+\left(\frac{\eta\mathcal{R}_0 S_{\mathrm{v}}}{\Lambda_{\mathrm{v}}}-1\right) I_h + \left(\frac{\gamma_2}{(\omega+\mu+\delta_h-\psi)}\right) R_h\\ &\leq \left[\frac{\upsilon\xi\sigma_h\Lambda_h}{\mu(\upsilon+\mu+\delta_h)(\omega+\mu+\delta_h-\psi)} - \frac{\eta(\alpha+\eta)(\eta+\delta_{\mathrm{v}})\mathcal{R}_0}{\xi\sigma_{\mathrm{v}}\Lambda_{\mathrm{v}}\alpha}\right] I_{\mathrm{v}} + (\mathcal{R}_0-1)\, I_h\end{aligned}$$

$$= \left[\left(\sqrt{\frac{\upsilon\sigma_h\Lambda_h\eta(\alpha+\eta)(\eta+\delta_{\mathrm{v}})}{\alpha\sigma_{\mathrm{v}}\Lambda_{\mathrm{v}}\mu(\upsilon+\mu+\delta_h)(\omega+\mu+\delta_h-\psi)}}\right) I_{\mathrm{v}} + I_h\right](\mathcal{R}_0-1)$$

If $\dot{\mathfrak{L}} \leq 0$ on condition that $\mathcal{R}_0 \leq 1$ in addition to $\dot{\mathfrak{L}} = 0$ as long as $\mathcal{R}_0 = 1$ or $I_h = 0$ and $I_{\mathrm{v}} = 0$ from the above result. It shows that the supreme invariance set in $\{(S_h, E_h, I_h, R_h, S_{\mathrm{v}}, E_{\mathrm{v}}, I_{\mathrm{v}}) \in \mathbb{R}^7_+ : \dot{\mathfrak{L}} = 0\}$ is the singleton disease free equilibrium (E_0). According to [9], Disease free equilibrium (E_0) is globally asymptotically stable in $\mathbb{R}^7_+$. □

3.3. Global Stability Analysis of Endemic Equilibrium

Theorem 3.2:
If $\mathcal{R}_0 > 1$, then equation (2.1) *has a unique endemic equilibrium, then $E_1 = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*)$ every time $\mathcal{R}_0 > 1$ and otherwise there is no endemic equilibrium.*

Proof
According to [4, 7, 10, 14], we have defined in eq. (3.3), the existence of EEP as $E_1 = (S_h^*, E_h^*, I_h^*, R_h^*, S_{\mathrm{v}}^*, E_{\mathrm{v}}^*, I_{\mathrm{v}}^*)$. It is assume that if $\epsilon_h = 0$ then the saturated incidence $\left(\frac{\xi\sigma_h I_{\mathrm{v}} S_h}{1+\epsilon_h I_{\mathrm{v}}}\right)$ becomes bilinear incidence $(\xi\sigma_h I_{\mathrm{v}} S_h)$. Similarly, if $\epsilon_{\mathrm{v}} = 0$ then the saturated incidence $\left(\frac{\xi\sigma_{\mathrm{v}} I_h S_{\mathrm{v}}}{1+\epsilon_{\mathrm{v}} I_h}\right)$ becomes bilinear incidence $(\xi\sigma_{\mathrm{v}} I_h S_{\mathrm{v}})$ [4,7,10,14]. Epidemiologically, it is assumed that, in humans, the rate of antibodies produced against the antigens of human is zero (i.e. $\epsilon_h = 0$) and in mosquitoes, the rate of antibodies produced against the antigens of mosquitoes is zero (i.e. $\epsilon_{\mathrm{v}} = 0$). Therefore, eq. (3.3) becomes;

$$\begin{aligned}&S_h^* = \frac{\Lambda_h+\gamma_1 R_h^*}{\mu+\xi\sigma_h I_{\mathrm{v}}^*}; \quad E_h^* = \frac{\xi\sigma_h I_{\mathrm{v}}^* S_h^*}{(\upsilon+\mu)}; \quad I_h^* = \frac{\upsilon E_h^* + \gamma_2 R_h^*}{\omega+\mu+\delta_h-\psi}; \quad R_h^* = \frac{\omega I_h^*}{\gamma_1+\mu+\gamma_2};\\ &S_{\mathrm{v}}^* = \frac{\Lambda_{\mathrm{v}}}{\eta+\beta_{\mathrm{v}}^*}; \qquad E_{\mathrm{v}}^* = \frac{\beta_{\mathrm{v}}^* S_{\mathrm{v}}^*}{(\alpha+\eta)}; \qquad I_{\mathrm{v}}^* = \frac{\alpha E_{\mathrm{v}}^*}{\eta+\delta_{\mathrm{v}}}\end{aligned} \tag{3.7}$$

Let

$$\beta_h^* = \xi\sigma_h I_{\mathrm{v}}^* \quad and \quad \beta_{\mathrm{v}}^* = \xi\sigma_{\mathrm{v}} I_h^* \tag{3.8}$$

From eq. (3.7) and eq. (3.8), make I_h^* subject of formula by substitution method to obtain

$$I_h^* = \frac{\left(\upsilon\Lambda_h a_6 + \upsilon\gamma_1\omega I_h^* + a_2\omega\gamma_2 I_h^*\right)\beta_h^* + a_2\mu\omega\gamma_2 I_h^*}{a_2 a_3 a_6(\mu + \beta_h^*)} \tag{3.9}$$

where $a_1 = \xi^2\upsilon\Lambda_h\sigma_h\Lambda_{\mathrm{v}}\sigma_{\mathrm{v}}\alpha$, $a_2 = (\upsilon + \mu)$, $a_3 = (\omega + \mu + \delta_h - \psi)$, $a_4 = (\alpha + \eta)$, $a_5 = (\eta + \delta_{\mathrm{v}})$ and $a_6 = (\gamma_1 + \gamma_2 + \mu)$. Similarly, From eq. (3.7) and eq. (3.8), β_h^* can also be written as

$$\beta_h^* = \frac{\xi^2\Lambda_{\mathrm{v}}\sigma_h\sigma_{\mathrm{v}}\alpha I_h^*}{(\eta + \delta_{\mathrm{v}})(\alpha + \eta)(\eta + \xi\sigma_{\mathrm{v}} I_h^*)} \tag{3.10}$$

Therefore, eq. (3.9) and eq. (3.10) can now be written as

$$\mathcal{P}_1 I_h^* + \mathcal{P}_2 = 0 \tag{3.11}$$

where $\mathcal{P}_1 = \left(a_3\eta\left(\upsilon\gamma_1\omega + a_2\gamma_2\omega - a_2 a_3 a_6\right)\mathcal{R}_0^2 + \xi\upsilon\Lambda_h\sigma_{\mathrm{v}}(\omega\gamma_2 - a_3 a_6)\right)$ and $\mathcal{P}_2 = \upsilon\Lambda_h\eta\left(a_3 a_6(\mathcal{R}_0^2 - 1) + \omega\gamma_2\right)$

From the above result, eq. (3.11) can be rewritten as $I_h^* = \dfrac{-\mathcal{P}_2}{\mathcal{P}_1} \leq 0$ if $\mathcal{P}_2 \geq 0$ at $\mathcal{R}_0 \leq 1$, and there is no endemic equilibrium. Furthermore, $I_h^* = \dfrac{\mathcal{P}_2}{\mathcal{P}_1} > 0$ if $\mathcal{P}_2 < 0$ at $\mathcal{R}_0 > 1$. Thus, $\exists$ an endemic equilibrium only at $\mathcal{R}_0 > 1$. This means that eq. (2.1) has a unique endemic which is non-negative equilibrium anytime $\mathcal{R}_0 > 1$. □

Theorem 3.3:
If $\mathcal{R}_0 > 1$, then E_1 which is the endemic equilibrium defined as $E_1 = (S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*, I_v^*)$ is globally asymptotically stable in the neighborhood of the region $\mathbb{R}_+^7$.

Proof
Let us construct Goh-Volterra type Lyapunov function [4, 7, 10, 14]:

$$\begin{aligned}\mathcal{G} =& S_h - S_h^* - S_h^*\ln\frac{S_h}{S_h^*} + E_h - E_h^* - E_h^*\ln\frac{E_h}{E_h^*} + c_1\left(I_h - I_h^* - I_h^*\ln\frac{I_h}{I_h^*}\right)\\ &+ c_2\left(S_{\mathrm{v}} - S_{\mathrm{v}}^* - S_{\mathrm{v}}^*\ln\frac{S_{\mathrm{v}}}{S_{\mathrm{v}}^*}\right) + c_3\left(E_{\mathrm{v}} - E_{\mathrm{v}}^* - E_{\mathrm{v}}^*\ln\frac{E_{\mathrm{v}}}{E_{\mathrm{v}}^*}\right) + c_4\left(I_{\mathrm{v}} - I_{\mathrm{v}}^* - I_{\mathrm{v}}^*\ln\frac{I_{\mathrm{v}}}{I_{\mathrm{v}}^*}\right)\end{aligned}$$

where $c_1 = \dfrac{\xi\sigma_h S_h^* I_{\mathrm{v}}^*}{\upsilon E_h^*}$ $c_2 = c_3 = \dfrac{\sigma_h S_h^* I_{\mathrm{v}}^*}{\sigma_{\mathrm{v}} S_{\mathrm{v}}^* I_h^*}$ and $c_4 = \dfrac{\xi\sigma_h S_h^* I_{\mathrm{v}}^*}{\alpha E_{\mathrm{v}}^*}$.
The derivation of $\mathcal{G}$ with respect to time is;

$$\begin{aligned}\dot{\mathcal{G}} =& \left(1 - \frac{S_h^*}{S_h}\right)\dot{S}_h + \left(1 - \frac{E_h^*}{E_h}\right)\dot{E}_h + \frac{\xi\sigma_h S_h^* I_{\mathrm{v}}^*}{\upsilon E_h^*}\left(1 - \frac{I_h^*}{I_h}\right)\dot{I}_h + \frac{\sigma_h S_h^* I_{\mathrm{v}}^*}{\sigma_{\mathrm{v}} S_{\mathrm{v}}^* I_h^*}\\ &\left(1 - \frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}\right)\dot{S}_{\mathrm{v}} + \frac{\sigma_h S_h^* I_{\mathrm{v}}^*}{\sigma_{\mathrm{v}} S_{\mathrm{v}}^* I_h^*}\left(1 - \frac{E_{\mathrm{v}}^*}{E_{\mathrm{v}}}\right)\dot{E}_{\mathrm{v}} + \frac{\xi\sigma_h S_h^* I_{\mathrm{v}}^*}{\alpha E_{\mathrm{v}}^*}\left(1 - \frac{I_{\mathrm{v}}^*}{I_{\mathrm{v}}}\right)\dot{I}_{\mathrm{v}}\end{aligned} \tag{3.12}$$

To simplify the eq. (3.3) and consider $R_h \to R_h^*$ as time, $t \to \infty$, then we have;

$$\begin{aligned}
\Lambda_h =& \xi\sigma_h S_h^* I_{\mathrm{v}}^* + \mu S_h^* \\
(\upsilon+\mu) =& \frac{\xi\sigma_h S_h^* I_{\mathrm{v}}^*}{E_h^*} \\
(\omega+\mu+\delta_h-\psi) =& \frac{\upsilon E_h^*}{I_h^*} \\
\Lambda_{\mathrm{v}} =& \xi\sigma_{\mathrm{v}} S_{\mathrm{v}}^* I_h^* + \eta S_{\mathrm{v}}^* \\
(\alpha+\eta) =& \frac{\xi\sigma_{\mathrm{v}} S_{\mathrm{v}}^* I_h^*}{E_{\mathrm{v}}^*} \\
(\eta+\delta_{\mathrm{v}}) =& \frac{\alpha E_{\mathrm{v}}^*}{I_{\mathrm{v}}^*}
\end{aligned} \tag{3.13}$$

Substituting eq. (2.1) and eq. (3.13) into eq. (3.12) when $(R_h \to R_h^*)$ as time, $t \to \infty$ to obtain

$$\begin{aligned}
\dot{\mathcal{G}} =& \mu S_h^*\left(2-\frac{S_h^*}{S_h}-\frac{S_h}{S_h^*}\right)+\xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{S_h^*}{S_h}\right)+\xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{S_h I_{\mathrm{v}} E_h^*}{S_h^* I_{\mathrm{v}}^* E_h}\right)+ \\
& \xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{I_h^* E_h}{I_h E_h^*}\right)+\frac{\eta\sigma_h S_h^* I_{\mathrm{v}}^*}{\sigma_{\mathrm{v}} I_h^*}\left(2-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}-\frac{S_{\mathrm{v}}}{S_{\mathrm{v}}^*}\right)+\xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}\right) \\
& +\xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{S_{\mathrm{v}} I_h E_{\mathrm{v}}^*}{S_{\mathrm{v}}^* I_h^* E_{\mathrm{v}}}\right)+\xi\sigma_h S_h^* I_{\mathrm{v}}^*\left(1-\frac{I_{\mathrm{v}}^* E_{\mathrm{v}}}{I_{\mathrm{v}} E_{\mathrm{v}}^*}\right)
\end{aligned} \tag{3.14}$$

Thus, this can be reduced to

$$\begin{aligned}
\dot{\mathcal{G}} =& \mu S_h^*\left(2-\frac{S_h^*}{S_h}-\frac{S_h}{S_h^*}\right)+\frac{\eta\sigma_h S_h^* I_{\mathrm{v}}^*}{\sigma_{\mathrm{v}} I_h^*}\left(2-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}-\frac{S_{\mathrm{v}}}{S_{\mathrm{v}}^*}\right)+\xi\sigma_h S_h^* I_{\mathrm{v}}^* \\
& \left(6-\frac{S_h^*}{S_h}-\frac{I_h^* E_h}{I_h E_h^*}-\frac{S_h I_{\mathrm{v}} E_h^*}{S_h^* I_{\mathrm{v}}^* E_h}-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}-\frac{I_{\mathrm{v}}^* E_{\mathrm{v}}}{I_{\mathrm{v}} E_{\mathrm{v}}^*}-\frac{S_{\mathrm{v}} I_h E_{\mathrm{v}}^*}{S_{\mathrm{v}}^* I_h^* E_{\mathrm{v}}}\right)
\end{aligned} \tag{3.15}$$

Finally, if Arithmetic mean (AM) $\geq$ Geometric mean (GM), then the following inequalities satisfy;

$$\begin{aligned}
& 2-\frac{S_h^*}{S_h}-\frac{S_h}{S_h^*}\leq 0, \quad 2-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}-\frac{S_{\mathrm{v}}}{S_{\mathrm{v}}^*}\leq 0, \\
& \left(6-\frac{S_h^*}{S_h}-\frac{I_h^* E_h}{I_h E_h^*}-\frac{S_h I_{\mathrm{v}} E_h^*}{S_h^* I_{\mathrm{v}}^* E_h}-\frac{S_{\mathrm{v}}^*}{S_{\mathrm{v}}}-\frac{I_{\mathrm{v}}^* E_{\mathrm{v}}}{I_{\mathrm{v}} E_{\mathrm{v}}^*}-\frac{S_{\mathrm{v}} I_h E_{\mathrm{v}}^*}{S_{\mathrm{v}}^* I_h^* E_{\mathrm{v}}}\right)\leq 0
\end{aligned} \tag{3.16}$$

As a result of this, $\dot{\mathcal{G}} \leq 0$ for $\mathcal{R}_0 > 1$. Thus, all the parameters are positive with $\dot{\mathcal{G}} = 0$ as long as $S_h = S_h^*$, $E_h = E_h^*$, $I_h = I_h^*$, $S_{\mathrm{v}} = S_{\mathrm{v}}^*$, $E_{\mathrm{v}} = E_{\mathrm{v}}^*$, $I_{\mathrm{v}} = I_{\mathrm{v}}^*$. In the meantime, $R_h \to R_h^*$ as time, $t \to \infty$ and so [9] the endemic equilibrium (E_1) is globally asymptotically stable whenever $\mathcal{R}_0 > 1$. □

3.4. Numerical Simulation

We conduct a numerical simulation using the developed model to explore the dynamics of malaria within the human population. Our simulation utilizes the Runge-Kutta 4 (R-K 4) scheme integrated into Maple 2016, with parameter values specified in Table 4.2 and initial conditions as described in reference [2]. Figures 3.2(a) to 3.2(g) shows the disease

trend in each population. The results indicate an active malaria outbreak. The decreasing human classes reflect the progression of the disease within the human population, while the increasing mosquito classes suggest that mosquitoes are becoming more infectious, increasing the risk of further transmission to humans. Effective control measures, such as mosquito control and treatment of infected individuals, may be needed to mitigate the outbreak.

4. SENSITIVITY ANALYSIS

4.1. Sensitivity Analysis of Basic Reproduction Number $\mathcal{R}_0$ parameters

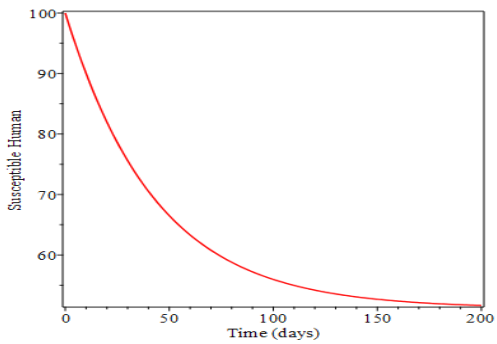
This model is of absolute imperative to examine the sensitivity analysis of the parameter standards. Sensitivity analysis can be used to determine which of the parameters from basic reproduction number $\mathcal{R}_0$ has more influence on the disease spread. According to [7–9,15,16], sensitivity index (S.I) analysis is an essential methodology for virtually all other sensitivity analysis approaches. This is also known as elasticity index. This can be done by using partial derivatives as soon as the variable is a differentiable function of the parameter. The normalized forward sensitivity index (S.I) of a variable or quantity $\mathcal{R}_0$ to a parameter α is a ratio of the relative change in the variable or quantity $\mathcal{R}_0$ to the relative change in the parameter α.

Theorem 4.1:
The normalized forward sensitivity index (S.I) of a variable or quantity $\mathcal{R}_0$ that depends differentiable on a parameter, α, is defined as:

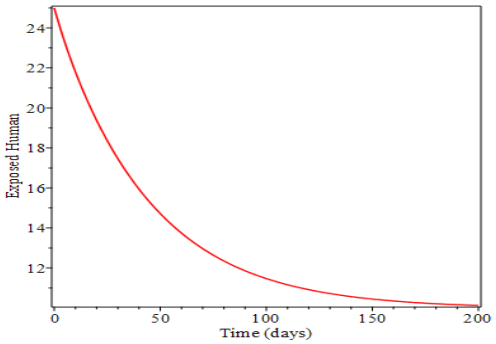
$$\mathbf{X}_{\theta}^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial \theta} \times \frac{\theta}{\mathcal{R}_0} \tag{4.17}$$

Sensitivity index of the parameters in eq. (3.4) is to use the formula in eq. (3.5). Therefore, the sensitivity index (S.I) for the parameters in eq. (3.4) can be written as follows:

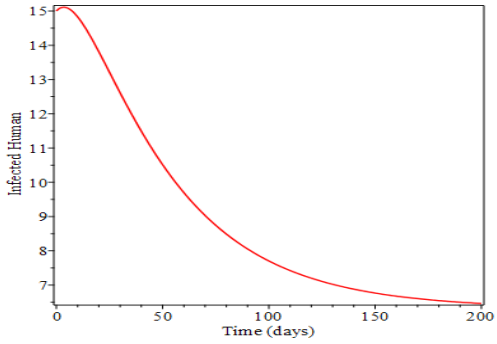
$$\begin{gathered}
\frac{\partial \mathcal{R}_0}{\partial \Lambda_h} \times \frac{\Lambda_h}{\mathcal{R}_0} = \frac{1}{2}, \qquad \frac{\partial \mathcal{R}_0}{\partial \Lambda_{\mathrm{v}}} \times \frac{\Lambda_{\mathrm{v}}}{\mathcal{R}_0} = \frac{1}{2}; \qquad \frac{\partial \mathcal{R}_0}{\partial \delta_h} \times \frac{\delta_h}{\mathcal{R}_0} = -\frac{\delta_h}{2(\omega+\mu+\delta_h-\psi)}; \\
\frac{\partial \mathcal{R}_0}{\partial \delta_{\mathrm{v}}} \times \frac{\delta_{\mathrm{v}}}{\mathcal{R}_0} = -\frac{\delta_{\mathrm{v}}}{2(\delta_{\mathrm{v}}+\eta)}; \qquad \frac{\partial \mathcal{R}_0}{\partial \psi} \times \frac{\psi}{\mathcal{R}_0} = \frac{\psi}{2(\omega+\mu+\delta_h-\psi)}; \\
\frac{\partial \mathcal{R}_0}{\partial \upsilon} \times \frac{\upsilon}{\mathcal{R}_0} = \frac{\mu}{2(\upsilon+\mu)}; \\
\frac{\partial \mathcal{R}_0}{\partial \mu} \times \frac{\mu}{\mathcal{R}_0} = \frac{1}{2}\frac{(2\mu\,(\psi-\omega-\upsilon-\delta_h)+\upsilon\;(\psi-\omega-\delta_h)-3\,\mu^2)}{(\upsilon+\mu)\,(\omega+\mu+\delta_h-\psi)}; \qquad \frac{\partial \mathcal{R}_0}{\partial \xi} \times \frac{\xi}{\mathcal{R}_0} = 1; \\
\frac{\partial \mathcal{R}_0}{\partial \sigma_h} \times \frac{\sigma_h}{\mathcal{R}_0} = \frac{1}{2}; \qquad \frac{\partial \mathcal{R}_0}{\partial \sigma_{\mathrm{v}}} \times \frac{\sigma_{\mathrm{v}}}{\mathcal{R}_0} = \frac{1}{2}; \qquad \frac{\partial \mathcal{R}_0}{\partial \alpha} \times \frac{\alpha}{\mathcal{R}_0} = \frac{\eta}{2(\alpha+\eta)}; \\
\frac{\partial \mathcal{R}_0}{\partial \omega} \times \frac{\omega}{\mathcal{R}_0} = -\frac{\omega}{2(\omega+\mu+\delta_h-\psi)}; \qquad \frac{\partial \mathcal{R}_0}{\partial \eta} \times \frac{\eta}{\mathcal{R}_0} = \frac{1}{2}\left(\frac{-3\,\eta^2-2\eta\,(\alpha+\delta_v)-\alpha\,\delta_v}{(\alpha+\eta)\,(\delta_v+\eta)}\right).
\end{gathered} \tag{4.18}$$



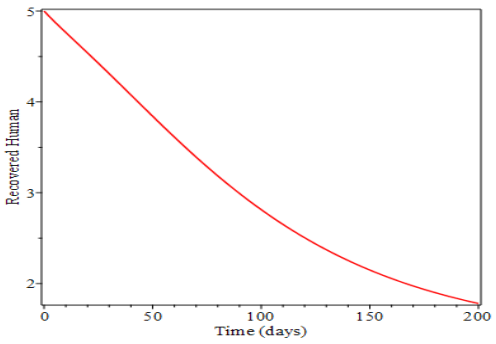
(a) The graph of Susceptible human against time



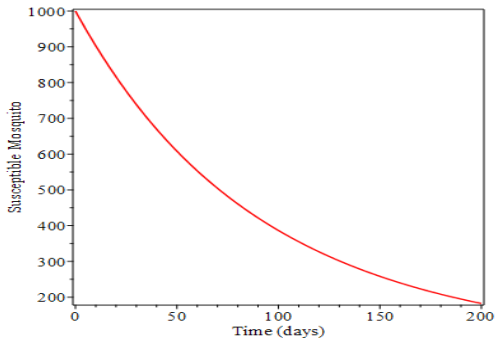
(b) The graph of Exposed human against time



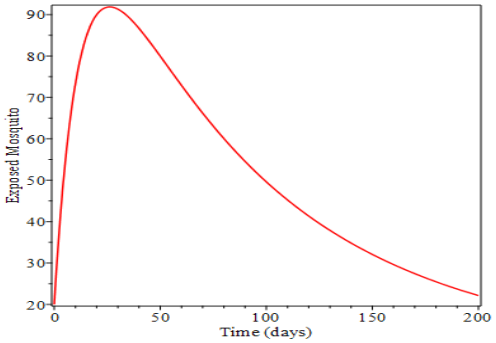
(c) The graph of Infected human against time



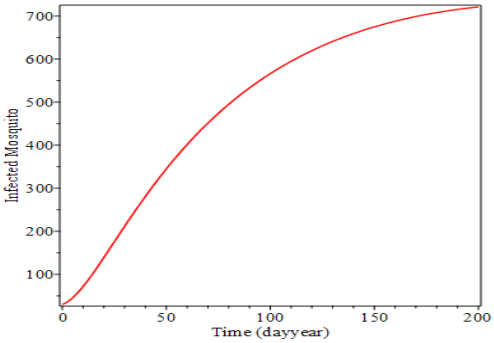
(d) The graph of Recovered human against time



(e) The graph of Susceptible mosquito against time



(f) The graph of Exposed mosquito against time



(g) The graph of Infected mosquito against time

Fig. 3.2. Disease dynamics

4.2. Tables of the Model and the Sensitivity Index

Table 4.1. The Model Variables and Descriptions

Variables	Description
$S_h(t)$	Number of susceptible humans at time t
$E_h(t)$	Number of exposed humans at time t
$I_h(t)$	Number of infectious humans at time t
$R_h(t)$	Number of recovered humans at time t
$S_{\mathrm{v}}(t)$	Number of susceptible mosquitoes at time t
$E_{\mathrm{v}}(t)$	Number of exposed mosquitoes at time t
$I_{\mathrm{v}}(t)$	Number of infectious mosquitoes at time t
$N_h(t)$	Total number of humans population at time t
$N_{\mathrm{v}}(t)$	Total number of mosquitoes population at time t

Table 4.2. Parameters, Descriptions Values and Sources

Parameter	Description	Value	Source
Λ_h	Recruitment rate of humans	1.2	[2]
Λ_{v}	Recruitment rate of mosquitoes	0.7	[2]
δ_h	Disease-induced death rate of humans	0.068	[2]
δ_{v}	Disease-induced death rate of mosquitoes	0.001	[2]
ψ	Rate of the newborn birth with infection humans	0.003	[2]
υ	Developing rate of exposed humans	0.05	[2]
μ	Natural Death of humans	0.01146	[2]
ξ	Biting rate of mosquitoes	0.12	[2]
α	Developing rate of exposed mosquitoes	0.083	[2]
η	Natural death rate of mosquitoes	0.00083	[2]
ε_h	Proportion of an antibody produced by human in response to the incidence of infection caused by mosquito	1.0	[2]
ε_{v}	Proportion of an antibody produced by mosquito in response to the incidence of infection caused by human	1.0	[2]
σ_h	Probability of transmission of infection from an infectious mosquitoes to a susceptible humans	0.1	[2]
σ_{v}	Probability of transmission of infection from an infectious humans to a susceptible mosquitoes	0.09	[2]
ω	Recovery rate of humans	0.0035	[2]
γ_1	Rate of loss of immunity in humans	0.00017	[2]
γ_2	Relapse rate of humans	0.04	[2]

4.3. Graphical Representation

The diagram below shows the graphical representation of the sensitivity analysis of each parameter present in the basic reproduction number.

4.4. Discussion of the Results

Table 4.3 shows the sensitivity index of the parameters by using basic reproduction number ($\mathcal{R}_0$) in eq. (3.4) and at the baseline parameter values in Table 4.2. The negative sign of sensitivity index shows that, by increasing the value of the parameters, this will reduce the value of $\mathcal{R}_0$ but for the positive sign of sensitivity index, it indicates that as parameter increases so also basic reproduction number $\mathcal{R}_0$. The most sensitive parameters with respect to the transmission of malaria from Table 4.3 is the biting rate of mosquitoes (ξ) with the sensitivity index equals to 1.0000 (S.I = 1.0000).

Table 4.3. Parameters, Descriptions and Sensitivity indexes of $\mathcal{R}_0$

Parameter	Description	Sensitivity Index
Λ_h	Recruitment rate of humans	0.5000
Λ_{v}	Recruitment rate of mosquitoes	0.5000
δ_h	Disease-induced death of humans	- 0.4252
δ_{v}	Disease-induced death of mosquitoes	- 0.2732
ψ	Rate of the newborn birth with infection humans	0.0188
υ	Exposed rate of humans to infectious class	0.0932
μ	Natural Death of humans	- 0.6649
ξ	Biting rate of mosquitoes	1.0000
α	Exposed rate of mosquitoes to infectious class	0.00495
η	Natural death rate of mosquitoes	- 0.7318
σ_h	Probability of transmission of infection from an infectious mosquitoes to a susceptible humans	0.5000
σ_{v}	Probability of transmission of infection from an infectious humans to a susceptible mosquitoes	0.5000
ω	Recovery rate of humans	-0.0219

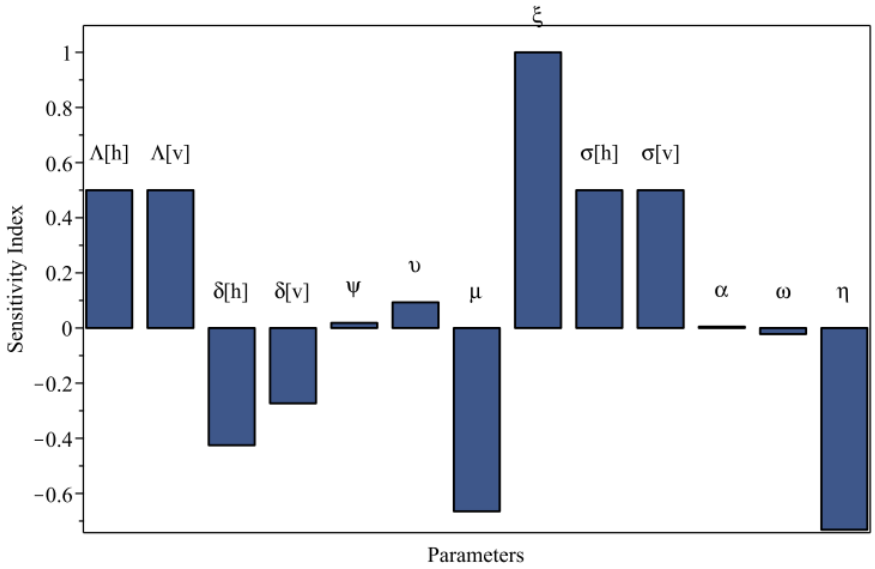


Fig. 4.3. Sensitivity Index against parameters

This shows that if there is 10% increase in the biting rate of mosquitoes, this will increase basic reproduction number ($\mathcal{R}_0$) by 10.00% as the respective index for the parameter is one. Next parameter to the most sensitive parameter due to the spread of malaria from Table 4.3 is the natural death rate of mosquitoes with the sensitivity index equals to - 0.7318 (S.I = - 0.7318). This shows that increasing the natural death rate of mosquitoes by 10% will result in increases in the value of $\mathcal{R}_0$ by 7.318%. Similarly, Table 4.3 is the natural death rate of humans with the sensitivity index equals to - 0.6649 (S.I = - 0.6649). This shows that increasing (or decreasing), the natural death rate of humans by 10% will increase or decrease $\mathcal{R}_0$ by 6.649%.

Moreover, the recruitment rates of humans (Λ_h) and mosquitoes (Λ_{v}) show that probabilities of transmission of infections from infectious mosquitoes to susceptible humans (σ_h), and from infectious humans to susceptible mosquitoes (σ_{v}) with the sensitivity index equal to 0.5000 (S.I = 0.5000). This shows that increasing or decreasing in each of these parameters by 10% increase or decrease in $\mathcal{R}_0$ in each of these parameters by 5%. Similarly,

Table 4.3 is the disease-induced death rate of humans (δ_h) with the sensitivity index equals to - 0.4252 (S.I = - 0.4252). This illustrates that increasing or decreasing the disease-induced death rate of humans by 10% will result in increase or decrease in $\mathcal{R}_0$ by 4.252%. Likewise, the disease-induced death rate of mosquitoes δ_{v} with the sensitivity index is equal to - 0.2732 (S.I = - 0.2732). This show that increasing or decreasing, disease-induced death rate of mosquitoes by 10% will increase or decrease the value of $\mathcal{R}_0$ by 2.732%. On the other hand, the other parameters sensitivity indices are very small which show that they have no impact on $\mathcal{R}_0$.

5. CONCLUSION

In conclusion, this study delved into a complex mathematical model of malaria, incorporating the crucial basic reproduction number ($\mathcal{R}_0$) and employing Lyapunov functions to assess the global stability of disease-free and endemic equilibria. Sensitivity analysis of key parameters provided insights into their role in disease control. The findings reveal an ongoing malaria outbreak characterized by declining human populations and increasing mosquito populations, signifying elevated transmission risk. The imperative response lies in implementing robust control measures, including mosquito management and prompt treatment of infected individuals, to effectively curb the outbreak and safeguard public health.

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