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Research article

Dynamics of a dengue disease transmission model with two-stage structure in the human population

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Abstract: Age as a risk factor is common in vector-borne infectious diseases. This is partly because children depend on adults to take preventative measures, and adults are less susceptible to mosquito bites because they generally spend less time outdoors than children. We propose a dengue disease model that considers the human population as divided into two subpopulations: children and adults. This is in order to take into consideration that children are more likely than adults to be bitten by mosquitoes. We calculated the basic reproductive number of dengue, using the next-generation operator method. We determined the local and global stability of the disease-free equilibrium. We obtained sufficient conditions for the global asymptotic stability of the endemic equilibrium using the Lyapunov functional method. When the infected periods in children and adults are the same, we that the endemic equilibrium is globally asymptotically stable in the interior of the feasible region when the threshold quantity $R_0 > 1$. Additionally, we performed a numerical simulation using parameter values obtained from the literature. Finally, a local sensitivity analysis was performed to identify the parameters that have the greatest influence on changes in (R_0), and thereby obtain a better biological interpretation of the results.

Keywords: host–vector model; dengue; children and adults; direct Lyapunov method; local sensitivity analysis

1. Introduction

In recent years, dengue has become a problem for health systems at the international level. According to the World Health Organization (WHO), approximately between 50–100 million cases of dengue occur annually. Around 3.9 million people in approximately 128 countries are at risk of suffering from this disease because they live in regions where it is endemic. These countries are mainly located in

regions of Africa, Asia, Oceania, and America where the geographic, demographic, and epidemiological conditions are conducive to the interaction between the vector, the virus, and the host. Dengue is transmitted by the bite of female mosquitoes, mainly of the species Aedes aegypti, after they become infected and after the minimum extrinsic incubation period has elapsed, which is 8 to 12 days before becoming infectious. The virus is injected into the human bloodstream by the mosquito bite and begins an incubation period for the disease that lasts from 4 to 10 days. After this time has elapsed, the infectious period of the host begins, starting the infectious process again [1].

For the study of viral dynamics, the mechanisms involved in the transmission of the pathogen between humans and vectors and the factors that influence the incidence of this disease, different mathematical models have been proposed in the language of ordinary differential equations (ODE). The results of such studies can aid the interventions by the health authorities.

In 1998, Esteva and Vargas [2] developed the first mathematical SIR-SI model for the dynamics of transmission of dengue fever that considers a constant human population.

Subsequently, Esteva and Vargas [3] formulated a system of differential equations that models the dynamics of transmission of dengue, where they consider a vertical and mechanical transmission in the vector population. Garba et al. [4] developed and rigorously analyzed a deterministic model for the dynamics of the transmission of dengue with or without imperfect vaccination, which exhibits a backward bifurcation.

Ghosh et al. [5] analyzed a compartmental model where the vector population is divided into three compartments: susceptible, exposed, and infected.

The human population is divided into seven compartments, within which two correspond to susceptible humans: those with low and high risk of getting infected. They assumed that the individuals in the low risk susceptible class have a lower chance of acquiring the infection as compared to the people in the high risk susceptible class.

For more details on the models in dengue, consult the systematic review conducted by Andraud et al. [6] in 2012, whose aim was to review the deterministic models of dengue transmission, and who identified 42 published models of interest, categorized into single serotype and multiserotype models.

Abidemi et al. [7] studied a two-strain compartmental dengue model that incorporates two control measures: Dengvaxia vaccine and insecticide. The same authors have studied other dengue model with multiple controls [8]. Asamoah et al. [9] analyzed a dengue transmission model in the presence of partial immunity and asymptomatic individuals with time-dependent controls.

They imposed time-dependent controls on their model: treated bednet, vaccination, treatment (prophylactics), and insecticides. Abidemi et al. [10] presented and analyzed a compartmental mathematical model that describes the dynamics of the transmission and control of dengue incorporating the effects of constant control rates. Abidemi et al. [11] developed and analyzed a model that captures the subpopulation of symptomatic infected human with severe dengue symptoms and Wolbachia-infected mosquito population.

There have been many studies of the incidence of dengue in children and adults. According to these studies, the most susceptible age groups vary, depending on the region. Siqueira Jr. et al. [12] studied dengue hemorrhagic fever (DHF) in Brazil and found that it primarily affected adults but noted an increase in cases in younger age groups. Huy et al. [13] performed an analysis of dengue data reported in Cambodia between the years 2002–2008, where they found that incidences by age were higher in infants under 1 year of age and children from 4 to 6 years old. In Thailand, dengue is more common

in older children [14, 15], while in Viet Nam the incidence is highest in children aged 6 to 10 years [16, 17]. In Malaysia and Singapore it is more common in 18 year olds [18, 19].

In 2016, Alera et al. [20] carried out a prospective longitudinal cohort study to determine the incidence of infection by the dengue virus in adults and children in the Philippines, where dengue is hyperendemic. They demonstrated that symptomatic dengue is primarily a pediatric disease in hyperendemic areas with a high force of infection.

In the reviewed literature on dengue models using ordinary differential equations, we identified some models that consider children and adults as different subpopulations. Aldila et al. [21] analyze an optimal control problem for a two-age-classes model, incorporating the implementation of mosquito repellent. Supriatna et al. [22] proposed a two-age-classes model with vaccination, because vaccination is usually concentrated in children. Chamnan et al. [23] developed a three-age-classes model with vaccination. The total population was subdivided into three groups: subjects less than 10 years old, between 10-44 years old, and those greater than 44 years old. This model ignores the terms of the transition from one age class to the next age class; this technical detail makes the constructions of the Lyapunov functions easier.

Although these dengue models take age groups into consideration, they have neglected the fact that adults are less susceptible to mosquito bites because they generally spend less time outdoors than children [24] and children are dependent upon adults for taking preventative measures. Translated into a measure of risk, we have that the relative risk of mosquito bites in adults versus children is less than unity. For this reason, we propose to analyze a two-stage-structure model that takes into consideration the differences in the risk of mosquito bites in children and adults.

This paper is organized as follows: in Section 2, we will propose a host–vector model with two-stage structure for dengue. In Section 3, we will compute the equilibria and basic reproductive number. In Section 4, we will study the local and global stability of disease-free equilibrium. In Section 5, we will determine the conditions for global asymptotic stability of the endemic equilibrium. In Section 6, we will present the results of numerical simulations for each of the scenarios of an outbreak of dengue. In Section 7, we will present the results of a local sensitivity analysis of the parameters on the threshold quantity (R_0). Finally, Section 8 contains the concluding remarks.

2. A two-stage-structure model in the human population

The proposed model is of the host–vector type, using ordinary differential equations (ODE) to describe the transmission of dengue; the population is considered to be constant.

The model has six compartments for the human population: susceptible children (S_C), susceptible adults (S_A), infected children (I_C), infected adults (I_A), recovered children (R_C), and recovered adults (R_A). The vector population has two compartments: susceptible (S_V) and infected (I_V).

The total population of humans is given by N_h, and μ_h is the rate of natural mortality. The parameter η denotes the rate at which children become part of the adult population. Since dengue infection is brief duration compared to the time a child reaches adulthood, for this reason, we do not incorporate the rate of maturation η from infected children to infected adults. We denote the contact rate that a virus-carrier mosquito has of susceptible children and adults by β_h/N_h and the incidence of new infections transmitted by the mosquitoes are given again by $\frac{\beta_h S_C I_V}{N_h}$ and $\frac{\sigma\beta_h S_A I_V}{N_h}$, respectively.

The parameter σ is the ratio between the probability that an adult is bitten by a mosquito and the

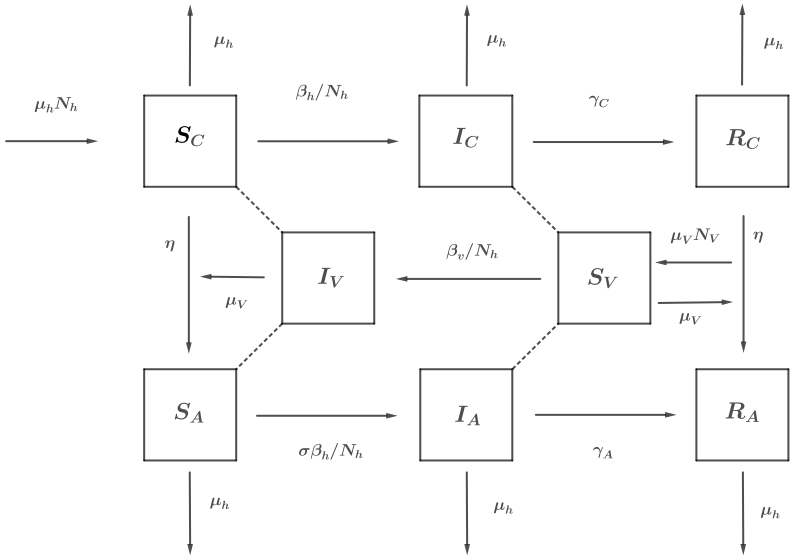

Figure 1. Schematic diagram of dengue disease transmission model with two-stage-structure in the human population.

probability that a child is bitten by a mosquito: it is the relative risk, and is assumed to be between zero and unity. Susceptible mosquitoes start carrying the virus after getting into contact with an infected human at a rate of β_v/N_h, so that the incidence of newly infected mosquitoes per infected children and adults is given by $\frac{\beta_v S_V I_C}{N_h}$ and $\frac{\sigma\beta_v S_V I_A}{N_h}$, respectively. The recovery rate for children and adults are given by γ_C and γ_A, respectively. The total mosquito population N_v is constant, and μ_v is the natural mortality rate of the mosquito. This dynamics can be represented by the compartmental diagram of Figure 1.

This model can be represented by the following system of ODEs:

$$\begin{aligned}
\frac{dS_C}{dt} &= \mu_h N_h - \frac{\beta_h}{N_h} S_C I_V - (\eta + \mu_h) S_C, \\
\frac{dS_A}{dt} &= \eta S_C - \sigma \frac{\beta_h}{N_h} S_A I_V - \mu_h S_A, \\
\frac{dI_C}{dt} &= \frac{\beta_h}{N_h} S_C I_V - (\gamma_C + \mu_h) I_C, \\
\frac{dI_A}{dt} &= \sigma \frac{\beta_h}{N_h} S_A I_V - (\gamma_A + \mu_h) I_A, \\
\frac{dR_C}{dt} &= \gamma_C I_C - (\eta + \mu_h) R_C, \\
\frac{dR_A}{dt} &= \eta R_C + \gamma_A I_A - \mu_h R_A, \\
\frac{dS_V}{dt} &= \mu_v N_V - \frac{\beta_v}{N_h} S_V (I_C + \sigma I_A) - \mu_v S_V, \\
\frac{dI_V}{dt} &= \frac{\beta_v}{N_h} S_V (I_C + \sigma I_A) - \mu_v I_V,
\end{aligned} \tag{2.1}$$

where it is assumed that $S_C + S_A + I_C + I_A + R_C + R_A = N_h$ and $S_V + I_V = N_V$ are the sizes of the human and vector populations, respectively.

Since $S_V = N_V - I_V$ and substituting in the last equation of (2.1), and since the variables $R_C(t)$ and $R_A(t)$ do not appear in the equations for $S_C(t)$, $I_C(t)$, $S_A(t)$ and $I_A(t)$ of system (2.1), it is sufficient to consider the behavior of the following system:

$$\begin{aligned}
\frac{dS_C}{dt} &= \mu_h N_h - \frac{\beta_h}{N_h} S_C I_V - (\eta + \mu_h) S_C, \\
\frac{dS_A}{dt} &= \eta S_C - \sigma \frac{\beta_h}{N_h} S_A I_V - \mu_h S_A, \\
\frac{dI_C}{dt} &= \frac{\beta_h}{N_h} S_C I_V - (\gamma_C + \mu_h) I_C, \\
\frac{dI_A}{dt} &= \sigma \frac{\beta_h}{N_h} S_A I_V - (\gamma_A + \mu_h) I_A, \\
\frac{dI_V}{dt} &= \frac{\beta_v}{N_h} (N_V - I_V)(I_C + \sigma I_A) - \mu_V I_V.
\end{aligned} \tag{2.2}$$

The feasible region of system (2.1) is given by,

$$\Omega = \left\{ (S_C, S_A, I_C, I_A, I_V) \in \mathbb{R}^5_+ : S_C + S_A + I_C + I_A \le N_h,\ I_V \le N_V,\ S_C \le \tfrac{\mu_h N_h}{\eta + \mu_h},\ S_A \le \tfrac{\eta N_h}{\eta + \mu_h} \right\}.$$

3. Preliminaries

3.1. Existence of equilibrium

Setting the equations of (2.2) equal to zero and expressing the variables S_C, S_A, I_C and I_A in terms of I_V, the equilibria of this system are obtained. Solving for S_C and S_A of the first and second equations, respectively, of (2.2), we obtain:

$$S_C = \frac{\mu_h N_h}{\frac{\beta_h}{N_h} I_V + \eta + \mu_h}, \tag{3.1}$$

$$S_A = \frac{\eta \mu_h N_h}{\left(\frac{\beta_h}{N_h} I_V + \eta + \mu_h\right)\left(\sigma \frac{\beta_h}{N_h} I_V + \mu_h\right)}. \tag{3.2}$$

Solving for I_C and I_A of the third and fourth equations in (2.2), respectively, we obtain:

$$I_C = \frac{\mu_h \beta_h I_V}{(\gamma_C + \mu_h)\left(\frac{\beta_h}{N_h} I_V + \eta + \mu_h\right)}, \tag{3.3}$$

$$I_A = \frac{\eta \sigma \mu_h \beta_h I_V}{(\gamma_A + \mu_h)\left(\frac{\beta_h}{N_h} I_V + \eta + \mu_h\right)\left(\sigma \frac{\beta_h}{N_h} I_v + \mu_h\right)}. \tag{3.4}$$

Assuming that $I_V = 0$, the disease-free equilibrium is

$$E_0 = \left(\frac{\mu_h N_h}{\eta + \mu_h}, \frac{\eta N_h}{\eta + \mu_h}, 0, 0, 0 \right), \tag{3.5}$$

which always exists in Ω.

To find the positive equilibrium in Ω, it must be assumed that $I_V \neq 0$. Substituting I_C and I_A in the fifth equation of (2.2), we perform various calculations, one obtains that I_V satisfies the following quadratic equation:

$$p(I_V) = aI_V^2 + bI_V + c, \tag{3.6}$$

where the coefficients are given by

$$a = -\left(\frac{\beta_h}{N_h}\right)^2 \left[\beta_v \mu_h \sigma(\gamma_A + \mu_h) + \mu_v \sigma(\gamma_C + \mu_h)(\gamma_A + \mu_h)\right], \tag{3.7}$$

$$\begin{aligned} b = {} & \frac{\beta_h \beta_v}{(N_h)^2} \mu_h (\gamma_A + \mu_h)(N_V \sigma \beta_h - \mu_h N_h) - \frac{\beta_h}{N_h} \beta_v \eta \mu_h \sigma^2 (\gamma_C + \mu_h) \\ & - \mu_v \frac{\beta_h}{N_h} (\gamma_C + \mu_h)(\gamma_A + \mu_h) \left[\mu_h + \sigma(\eta + \mu_h)\right], \end{aligned} \tag{3.8}$$

$$c = \mu_h \mu_v (\eta + \mu_h)(\gamma_C + \mu_h)(\gamma_A + \mu_h)(R_0 - 1), \tag{3.9}$$

where R_0 is a threshold value and is given by

$$R_0 = \frac{\beta_h \beta_v N_V \mu_h}{\mu_v N_h (\eta + \mu_h)(\gamma_C + \mu_h)} + \frac{\sigma^2 \beta_h \beta_v N_V \eta}{\mu_v N_h (\eta + \mu_h)(\gamma_A + \mu_h)}. \tag{3.10}$$

Since all the parameters of the model are positive, it can be seen that the coefficient a is negative. Accordingly, the quadratic equation (3.6) is concave down. In (3.11), all the parameters are positive, if $R_0 > 1$, then $p(0) > 0$, so that (3.6) has only one positive solution.

$$p(0) = c = \mu_h \mu_v (\eta + \mu_h)(\gamma_C + \mu_h)(\gamma_A + \mu_h)(R_0 - 1). \tag{3.11}$$

With these results, the following lemma can be asserted.

Lemma 3.1. *Let R_0 be defined by (3.10). If $R_0 \leq 1$, then only the disease-free equilibrium E_0 exists in Ω. If $R_0 > 1$, then there is a disease-free equilibrium in Ω and a unique endemic equilibrium $E^* = (S_C^*, S_A^*, I_C^*, I_A^*, I_V^*)$ in int(Ω) whose coordinates are given by equations (3.1)–(3.4) and the positive solution of (3.6).*

3.2. Basic reproductive number

We obtain the basic reproductive number $\hat{R}_0$ using the next generation method [25, 26]. The Jacobian matrix J of this subsystem at the disease-free equilibrium is decomposed as $J = F - V$, where F is the transmission part and V describe the transition terms associated with the model (2.2). These quantities are given, respectively, by

$$F = \begin{bmatrix} 0 & 0 & \frac{\beta_h \mu_h}{\eta + \mu_h} \\ 0 & 0 & \frac{\sigma \beta_h \eta}{\eta + \mu_h} \\ \frac{\beta_v}{N_h} N_V & \sigma \frac{\beta_V}{N_h} N_V & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \gamma_C + \mu_h & 0 & 0 \\ 0 & \gamma_A + \mu_h & 0 \\ 0 & 0 & \mu_v \end{bmatrix}.$$

Now, the values of F and V are calculated because the basic reproductive number is given by $\rho(FV^{-1})$, where ρ is defined as the spectral radius:

$$\hat{R}_0 = \sqrt{\frac{\beta_h \beta_v N_V}{\mu_v N_h(\eta + \mu_h)}\left(\frac{\mu_h}{\gamma_C + \mu_h} + \frac{\sigma^2 \eta}{\gamma_A + \mu_h}\right)}. \tag{3.12}$$

This threshold is $\hat{R}_0$, and is the square root of R_0, but both give the equivalent condition $R_0 > 1$ (or $R_0 \leq 1$) $\Leftrightarrow \hat{R}_0 > 1$ (or $\hat{R}_0 \leq 1$). For the rest of this paper, we will use the threshold number R_0 as the basis for the analysis.

The expression for $\hat{R}_0$ represents the average of the secondary infections generated by a primary case when introduced in a whole susceptible human population. This can be seen as follows: an infected mosquito distributes bites in the human population for the rest of its life, and a proportion $\frac{\beta_h N_V}{\mu_v N_h}$ of these bites becomes new infections. On the other hand, the number of new infections of mosquitoes by infected children and infected adults during the infectious period is given by $\frac{\beta_v}{\eta+\mu_h}(\frac{\mu_h}{\gamma_C+\mu_h} + \frac{\sigma^2\eta}{\gamma_A+\mu_h})$, respectively. The geometric mean of these two quantities, which is equal to $\hat{R}_0$, gives the average number of secondary infections.

4. Stability of disease-free equilibrium

In this section the stability properties of the disease-free equilibrium will be analyzed.

Theorem 4.1. *i) If $R_0 < 1$, then the disease-free equilibrium E_0 is local asymptotically stable. ii) If $R_0 > 1$, then the disease-free equilibrium E_0 is unstable.*

Proof. The Jacobian matrix of system (2.2) is given by

$$J = \begin{bmatrix} -\frac{\beta_h}{N_h} I_V - (\eta + \mu_h) & 0 & 0 & 0 & -\frac{\beta_h}{N_h} S_C \\ \eta & -\sigma\frac{\beta_h}{N_h} I_V - \mu_h & 0 & 0 & -\sigma\frac{\beta_h}{N_h} S_A \\ \frac{\beta_h}{N_h} I_V & 0 & -(\gamma_C + \mu_h) & 0 & \frac{\beta_h}{N_h} S_C \\ 0 & \sigma\frac{\beta_h}{N_h} I_V & 0 & -(\gamma_A + \mu_h) & \sigma\frac{\beta_h}{N_h} S_A \\ 0 & 0 & \frac{\beta_v}{N_h}(N_V - I_V) & \sigma\frac{\beta_v}{N_h}(N_V - I_V) & -\frac{\beta_v}{N_h}(I_C + \sigma I_A) - \mu_v \end{bmatrix} \tag{4.1}$$

The local stability of the disease-free equilibrium E_0 depends on the eigenvalues of the matrix:

$$J(E_0) = \begin{bmatrix} -(\eta+\mu_h) & 0 & 0 & 0 & -\frac{\beta_h\mu_h}{\eta+\mu_h} \\ \eta & -\mu_h & 0 & 0 & \frac{-\sigma\beta_h\eta}{\eta+\mu_h} \\ 0 & 0 & -(\gamma_C+\mu_h) & 0 & \frac{\beta_h\mu_h}{\eta+\mu_h} \\ 0 & 0 & 0 & -(\gamma_A+\mu_h) & \frac{\sigma\beta_h\eta}{\eta+\mu_h} \\ 0 & 0 & \frac{\beta_v}{N_h}N_V & \sigma\frac{\beta_v}{N_h}N_V & -\mu_v \end{bmatrix} \tag{4.2}$$

where, clearly, the eigenvalues are $-\mu_h$, $-(\eta+\mu_h)$ and those obtained from the matrix

$$P = \begin{bmatrix} -(\gamma_C+\mu_h) & 0 & \frac{\beta_h\mu_h}{\eta+\mu_h} \\ 0 & -(\gamma_A+\mu_h) & \frac{\sigma\beta_h\eta}{\eta+\mu_h} \\ \frac{\beta_v}{N_h}N_V & \sigma\frac{\beta_v}{N_h}N_V & -\mu_v \end{bmatrix} \tag{4.3}$$

The characteristic polynomial of P would be the following cubic equation,

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0, \tag{4.4}$$

where:

$$A = tr(P),$$

$$B = \begin{vmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{vmatrix} + \begin{vmatrix} a_{11} & a_{13} \\ a_{31} & a_{33} \end{vmatrix} + \begin{vmatrix} a_{22} & a_{23} \\ a_{32} & a_{33} \end{vmatrix},$$

$$C = -det(P).$$

After some calculations, we get

$$A = (\gamma_C+\mu_h) + (\gamma_A+\mu_h) + \mu_v, \tag{4.5}$$

$$\begin{aligned} B = {} & (\gamma_C+\mu_h)(\gamma_A+\mu_h) + (\gamma_C+\mu_h)\tfrac{\beta_h\beta_v N_V\sigma^2\eta}{N_h(\gamma_A+\mu_h)(\eta+\mu_h)} \\ & + (\gamma_A+\mu_h)\tfrac{\beta_h\beta_v\mu_h N_V}{N_h(\gamma_C+\mu_h)(\eta+\mu_h)} + \mu_v((\gamma_C+\mu_h)+(\gamma_A+\mu_h))(1-R_0), \end{aligned} \tag{4.6}$$

$$C = \mu_v(\gamma_A+\mu_h)(\gamma_C+\mu_h)(1-R_0). \tag{4.7}$$

Note that $A > 0$, and also that $R_0 < 1$ implies $B > 0$ and $C > 0$. Also,

$$A \cdot B > \mu_v(\gamma_C+\mu_h)(\gamma_A+\mu_h) > C,$$

which implies that $A \cdot B - C > 0$, and by the Routh–Hurwitz conditions, eigenvalues have negative real parts and consequently the disease-free equilibrium E_0 will be asymptotically stable. On the other hand, by Descarte's rule of signs, if $R_0 > 1$, then $C < 0$ and the polynomial (4.4) will have a positive eigenvalue, in which case E_0 will be unstable. □

Using a comparison theorem [27], we shall prove the global stability of the disease-free equilibrium for $R_0 < 1$. Following the idea used by Esteva et al. [28], we carry out the following proof.

Theorem 4.2. *If $R_0 < 1$, then E_0 is globally asymptotically stable in Ω.*

Proof. The equations for I_C, I_A and I_V of model (2.2) are

$$\begin{aligned} \frac{dI_C}{dt} &= \frac{\beta_h}{N_h} S_C I_V - (\gamma_C + \mu_h) I_C, \\ \frac{dI_A}{dt} &= \sigma \frac{\beta_h}{N_h} S_A I_V - (\gamma_A + \mu_h) I_A, \\ \frac{dI_V}{dt} &= \frac{\beta_v}{N_h} (N_V - I_V)(I_C + \sigma I_A) - \mu_v I_V. \end{aligned} \tag{4.8}$$

Since $S_C \leq \frac{\mu_h N_h}{\eta + \mu_h}$, $S_A \leq \frac{\eta N_h}{\eta + \mu_h}$ and $I_V \geq 0$, the equations of (4.8) satisfy the following:

$$\frac{d}{dt} \begin{pmatrix} I_C \\ I_A \\ I_V \end{pmatrix} \leq (F - V) \begin{pmatrix} I_C \\ I_A \\ I_V \end{pmatrix}, \tag{4.9}$$

where F and V were defined above.

If $R_0 < 1$, then $\rho(FV^{-1}) < 1$, which is equivalent to $F - V$ having all its eigenvalues in the left half-plane. This means that the linear system $\bar{Z}' = (F - V)\bar{Z}(t)$, where $\bar{Z} = (I_C(t), I_A(t), I_V(t))$, is asymptotically stable for $R_0 < 1$, and consequently the solutions of this system tend to zero as t approaches infinity. This means that the solutions of (2.2) corresponding to I_C, I_A and I_V approach zero as $t \to \infty$. Therefore, it can be concluded that the disease-free equilibrium is globally asymptotically stable for $R_0 < 1$ in the region Ω. □

5. Conditions for the global stability of the endemic equilibrium

In the following, we consider the global asymptotic stability of a unique endemic equilibrium E^*. Motivated by the classic work of Korobeinikov [29, 30] and Vargas-De-León [31, 32] in host–vector models, we construct a Lyapunov function for an endemic equilibrium, using Volterra-type functions $W(t) = x(t) - 1 - \ln x(t)$.

Theorem 5.1. *Let $R_0 > 1$. If*

$$\frac{1}{\gamma_C + \mu_h} \geq \frac{\sigma}{\gamma_A + \mu_h}, \tag{5.1}$$

then the endemic equilibrium E^* of (2.2) is globally asymptotically stable in int(Ω).

Proof. Define $L : int(\mathbb{R}^5_+) \to \mathbb{R}_+$

$$
\begin{aligned}
L(t) = {} & \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)S_C^* W\left(\frac{S_C}{S_C^*}\right) + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)S_A^* W\left(\frac{S_A}{S_A^*}\right) \\
& + \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)I_C^* W\left(\frac{I_C}{I_C^*}\right) + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)I_A^* W\left(\frac{I_A}{I_A^*}\right) \\
& + (\gamma_C + \mu_h)(\gamma_A + \mu_h)I_V^* W\left(\frac{I_V}{I_V^*}\right).
\end{aligned}
$$

The function $L(t)$ is defined, continuous and positive definite for all $S_C, S_A, I_C, I_A, I_V \geq 0$. Also, the global minimum $L(S_C, S_A, I_C, I_A, I_V) = 0$ occurs at $E^* = (S_C^*, S_A^*, I_C^*, I_A^*, I_V^*)$, and, therefore, L is a Lyapunov function. Calculating its derivative along the solution of (2.2) we obtain

$$
\begin{aligned}
\frac{dL}{dt} = {} & \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)\left(1 - \frac{S_C^*}{S_C}\right)\left[\mu_h N_h - \frac{\beta_h}{N_h}S_C I_V - (\eta + \mu_h)S_C\right] \\
& + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)\left(1 - \frac{S_A^*}{S_A}\right)\left[\eta S_C - \sigma\frac{\beta_h}{N_h}S_A I_V - \mu_h S_A\right] \\
& + \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)\left(1 - \frac{I_C^*}{I_C}\right)\left[\frac{\beta_h}{N_h}S_C I_V - (\gamma_C + \mu_h)I_C\right] \\
& + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)\left(1 - \frac{I_A^*}{I_A}\right)\left[\sigma\frac{\beta_h}{N_h}S_A I_V - (\gamma_A + \mu_h)I_A\right] \\
& + (\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(1 - \frac{I_V^*}{I_V}\right)\left[\frac{\beta_v}{N_h}(N_V - I_V^*)I_C + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)I_A - \mu_v I_V\right] \\
& + (\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(1 - \frac{I_V^*}{I_V}\right)\left[\frac{\beta_v}{N_h}I_V^*\left(1 - \frac{I_V}{I_V^*}\right)(I_C + \sigma I_A)\right].
\end{aligned}
$$

At an endemic equilibrium, we have

$$
\mu_h N_h = \mu_h S_C^* + \mu_h S_A^* + (\gamma_C + \mu_h)I_C^* + (\gamma_A + \mu_h)I_A^*, \tag{5.2}
$$

$$
\eta = \frac{\mu_h S_A^*}{S_C^*} + \frac{(\gamma_A + \mu_h)I_A^*}{S_C^*}, \tag{5.3}
$$

$$
\frac{\beta_h}{N_h} = (\gamma_C + \mu_h)\frac{I_C^*}{S_C^* I_V^*}, \tag{5.4}
$$

$$
\sigma\frac{\beta_h}{N_h} = (\gamma_A + \mu_h)\frac{I_A^*}{S_A^* I_V^*}, \tag{5.5}
$$

$$
\mu_v = \frac{\beta_v}{N_h}\frac{(N_V - I_V^*)I_C^*}{I_V^*} + \frac{\sigma\beta_v}{N_h}\frac{(N_V - I_V^*)I_A^*}{I_V^*}. \tag{5.6}
$$

Using (5.2)–(5.6), we obtain

$$
\frac{dL}{dt} = \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)\left(1 - \frac{S_C^*}{S_C}\right)\left[\mu_h S_C^* + \mu_h S_A^* + (\gamma_C + \mu_h)I_C^* + (\gamma_A + \mu_h)I_A^* - (\gamma_C + \mu_h)I_C^*\frac{S_C I_V}{S_C^* I_V^*}\right]
$$

$$
\begin{aligned}
&- \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)\left(1 - \frac{S_C^*}{S_C}\right)\left[\left\{\frac{\mu_h S_A^*}{S_C^*} + \frac{(\gamma_A + \mu_h)I_A^*}{S_C^*}\right\} S_C + \mu_h S_C\right] \\
&+ \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)\left(1 - \frac{S_A^*}{S_A}\right)\left[\left(\frac{\mu_h S_A^*}{S_C^*} + \frac{(\gamma_A + \mu_h)I_A^*}{S_C^*}\right) S_C - (\gamma_A + \mu_h)I_A^*\frac{S_A I_V}{S_A^* I_V^*} - \mu_h S_A\right] \\
&+ \frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_A + \mu_h)\left(1 - \frac{I_C^*}{I_C}\right)\left[(\gamma_C + \mu_h)I_C^*\frac{S_C I_V}{S_C^* I_V^*} - (\gamma_C + \mu_h)I_C\right] \\
&+ \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)(\gamma_C + \mu_h)\left(1 - \frac{I_A^*}{I_A}\right)\left[(\gamma_A + \mu_h)I_A^*\frac{S_A I_V}{S_A^* I_V^*} - (\gamma_A + \mu_h)I_A\right] \\
&+ (\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(1 - \frac{I_V^*}{I_V}\right)\left[\frac{\beta_v}{N_h}(N_V - I_V^*)I_C + \sigma\frac{\beta_v}{N_h}(N_V - I_V^*)I_A\right] \\
&- (\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(1 - \frac{I_V^*}{I_V}\right)\left[\left\{\frac{\beta_v}{N_h}\frac{(N_V - I_V^*)I_C^*}{I_V^*} + \frac{\sigma\beta_v}{N_h}\frac{(N_V - I_V^*)I_A^*}{I_V^*}\right\} I_V\right] \\
&+ (\gamma_C + \mu_h)(\gamma_A + \mu_h)\frac{\beta_v}{N_h}I_V^*\left(2 - \frac{I_V^*}{I_V} - \frac{I_V}{I_V^*}\right)(I_C + \sigma I_A), \\
&= \frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_A + \mu_h)(\mu_h S_C^* + \mu_h S_A^* + (\gamma_A + \mu_h)I_A^*)\left(2 - \frac{S_C}{S_C^*} - \frac{S_C^*}{S_C}\right) \\
&+ \frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_A + \mu_h)(\gamma_C + \mu_h)I_C^*\left(1 - \frac{S_C I_V}{S_C^* I_V^*} - \frac{S_C^*}{S_C} + \frac{I_V}{I_V^*}\right) \\
&+ \mu_h S_A^*\sigma\frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_C + \mu_h)\left(\frac{S_C}{S_C^*} - \frac{S_A}{S_A^*} - \frac{S_A^*}{S_A}\frac{S_C}{S_C^*} + 1\right) \\
&+ (\gamma_A + \mu_h)I_A^*\sigma\frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_C + \mu_h)\left(\frac{S_C}{S_C^*} - \frac{S_A I_V}{S_A^* I_V^*} - \frac{S_A^*}{S_A}\frac{S_C}{S_C^*} + \frac{I_V}{I_V^*}\right) \\
&+ \frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_A + \mu_h)(\gamma_C + \mu_h)I_C^*\left(\frac{S_C I_V}{S_C^* I_V^*} - \frac{I_C}{I_C^*} - \frac{I_C^*}{I_C}\frac{S_C I_V}{S_C^* I_V^*} + 1\right) \\
&+ \sigma\frac{\beta_v}{N_h}[N_V - I_V^*](\gamma_C + \mu_h)(\gamma_A + \mu_h)I_A^*\left(\frac{S_A I_V}{S_A^* I_V^*} - \frac{I_A}{I_A^*} - \frac{I_A^*}{I_A}\frac{S_A I_V}{S_A^* I_V^*} + 1\right) \\
&+ \frac{\beta_v}{N_h}I_C^*[N_V + I_V^*](\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(\frac{I_C}{I_C^*} - \frac{I_V}{I_V^*} - \frac{I_V^*}{I_V}\frac{I_C}{I_C^*} + 1\right) \\
&+ \sigma\frac{\beta_v}{N_h}I_A^*[N_V - I_V^*](\gamma_C + \mu_h)(\gamma_A + \mu_h)\left(\frac{I_A}{I_A^*} - \frac{I_V}{I_V^*} - \frac{I_V^*}{I_V}\frac{I_A}{I_A^*} + 1\right) \\
&+ (\gamma_C + \mu_h)(\gamma_A + \mu_h)\frac{\beta_v}{N_h}I_V^*\left(2 - \frac{I_V^*}{I_V} - \frac{I_V}{I_V^*}\right)(I_C + \sigma I_A).
\end{aligned}
$$

After several calculations, the following expression is obtained:

$$
\begin{aligned}
\frac{dL}{dt} &= \frac{\beta_v I_C^*(N_V - I_V^*)}{N_h}[\mu_h S_C^*(\gamma_A + \mu_h) + ((\gamma_A + \mu_h) - \sigma(\gamma_C + \mu_h))(\mu_h S_A^* + (\gamma_A + \mu_h)I_A^*)]\left(2 - \frac{S_C^*}{S_C} - \frac{S_C}{S_C^*}\right) \\
&+ \frac{\beta_v I_C^*(N_V - I_V^*)}{N_h}(\gamma_C + \mu_h)(\gamma_A + \mu_h)\left[3 - \frac{S_C I_V I_C^*}{S_C^* I_V^* I_C} - \frac{I_C I_V^*}{I_C^* I_V} - \frac{S_C^*}{S_C}\right]
\end{aligned}
$$

$$+\frac{\sigma\beta_v I_A^*(N_V-I_V^*)}{N_h}(\gamma_C+\mu_h)(\gamma_A+\mu_h)\left[4-\frac{S_A I_V I_A^*}{S_A^* I_V^* I_A}-\frac{I_A I_V^*}{I_A^* I_V}-\frac{S_C S_A^*}{S_C^* S_A}-\frac{S_C^*}{S_C}\right]$$
$$+\mu_h S_A^*\frac{\sigma\beta_v(N_V-I_V^*)}{N_h}(\gamma_C+\mu_h)\left[3-\frac{S_C S_A^*}{S_C^* S_A}-\frac{S_A}{S_A^*}-\frac{S_C^*}{S_C}\right]$$
$$+\frac{\beta_v}{N_h}I_V^*(\gamma_C+\mu_h)(\gamma_A+\mu_h)\left(2-\frac{I_V^*}{I_V}-\frac{I_V}{I_V^*}\right)(I_C+\sigma I_A).$$

Rewriting the Korobeinikov-type functions as Volterra-type functions, we have

$$\frac{dL}{dt}=-\frac{\beta_v I_C^*(N_V-I_V^*)}{N_h}\left[\mu_h S_C^*(\gamma_A+\mu_h)+((\gamma_A+\mu_h)-\sigma(\gamma_C+\mu_h))(\mu_h S_A^*+(\gamma_A+\mu_h)I_A^*)\right]\left[W\left(\frac{S_C^*}{S_C}\right)+W\left(\frac{S_C}{S_C^*}\right)\right]$$
$$-\frac{\beta_v I_C^*(N_V-I_V^*)}{N_h}(\gamma_C+\mu_h)(\gamma_A+\mu_h)\left[W\left(\frac{S_C I_V I_C^*}{S_C^* I_V^* I_C}\right)+W\left(\frac{I_C I_V^*}{I_C^* I_V}\right)+W\left(\frac{S_C^*}{S_C}\right)\right]$$
$$-\frac{\sigma\beta_v I_A^*(N_V-I_V^*)}{N_h}(\gamma_C+\mu_h)(\gamma_A+\mu_h)\left[W\left(\frac{S_A I_V I_A^*}{S_A^* I_V^* I_A}\right)+W\left(\frac{I_A I_V^*}{I_A^* I_V}\right)+W\left(\frac{S_C S_A^*}{S_C^* S_A}\right)+W\left(\frac{S_C^*}{S_C}\right)\right]$$
$$-\mu_h S_A^*\frac{\sigma\beta_v(N_V-I_V^*)}{N_h}(\gamma_C+\mu_h)\left[W\left(\frac{S_C S_A^*}{S_C^* S_A}\right)+W\left(\frac{S_A}{S_A^*}\right)+W\left(\frac{S_C^*}{S_C}\right)\right]$$
$$-\frac{\beta_v}{N_h}I_V^*(\gamma_C+\mu_h)(\gamma_A+\mu_h)\left[W\left(\frac{I_V^*}{I_V}\right)+W\left(\frac{I_V}{I_V^*}\right)\right](I_C+\sigma I_A).$$

If condition (5.1) is satisfied, then $dL/dt \le 0$. Note that $dL/dt = 0$ if and only if $S_C = S_C^*$, $S_A = S_A^*$, $I_C = I_C^*$, $I_A = I_A^*$ and $I_V = I_V^*$. Therefore the largest compact invariant set in $\{(S_C(t), S_A(t), I_C(t), I_A(t), I_V(t)) : dL/dt = 0\}$ is the singleton $\{E^*\}$. If $R_0 > 1$ and $\frac{1}{\gamma_C+\mu_h} \ge \frac{\sigma}{\gamma_A+\mu_h}$, by the classical LaSalle invariance principle (Theorem 5.3 of [33]), the endemic equilibrium E^* is globally asymptotically stable in Ω. The theorem is proved. □

Assuming that the recovery rate from dengue is the same for children and adults [34], then we can state the following corollary.

Corollary 1. *Assume that $\gamma_A = \gamma_C$. If $R_0 > 1$, then the endemic equilibrium E^* of (2.2) is globally asymptotically stable in int(Ω).*

6. Numerical simulations

In this section, we present the results of numerical simulations used to visualise the trajectories of model (2.2). The time courses of the populations of children and adults were obtained by numerical integration using the method *Tsist5* [37] based on Runge–Kutta methods implemented by the DifferentialEquations.jl native package of the *Julia* ecosystem. We used a set of demographic and epidemiological parameters reported in the literature [21, 35, 36]. All the parameters involved in model (2.2) are summarized in Table 1.

In Figure 2, the numerical simulations show that the solutions converge to a disease-free equilibrium E_0. It can be seen that in the first weeks there is a greater number of cases of infected people, but

Table 1. Demographic and epidemiological parameters of dengue disease.

Parameter	Definition	Value	Ref
N_h	Total human population	15544639	Assumed
N_V	Total vector population	$3 \times N_h$	[35]
μ_h	Human mortality rate	$\frac{1}{76\times52}$ week^{-1}	Assumed
μ_v	Vector mortality rate	$\frac{1}{2}$ week^{-1}	[36]
β_h	Probability of vector to human transmission	[0, 1]	Vary
β_v	Probability of human to vector transmission	[0, 1]	Vary
γ_C	Child recovery rate	$\frac{1}{2}$ week^{-1}	[21]
γ_A	Adult recovery rate	$\frac{1}{2}$ week^{-1}	[21]
η	Rate at which children pass into adulthood	$\frac{1}{20\times52}$ week^{-1}	[21]

then they decrease rapidly until they disappear. The values of the parameters are as in Table 1, and $\sigma = \frac{1}{3}$, $\beta_h = \frac{1}{2}$ and $\beta_v = \frac{1}{2}$. The initial conditions used are: $S_C(0) = 3\ 238\ 466$, $S_A(0) = 1\ 230\ 617$, $I_C(0) = 0$, $I_A(0) = 0$, $I_V(0) = 3000$. With these parameter values, $R_0 = 0.88$, this is the scenario where only a disease-free equilibrium exists, and it is locally and globally asymptotically stable according to Theorems 4.1 and 4.2, respectively.

In Figure 3, the numerical simulations illustrate that the solutions converge to an endemic equilibrium E^*. It can be seen that several outbreaks occur over a period of three thousand weeks, but each outbreak will have a lower number of cases than the previous one. The values of the parameters and the initial conditions are the same as in Figure 2, except for the parameters $\sigma = \frac{1}{3}$, $\beta_h = \frac{3}{4}$ and $\beta_v = \frac{3}{4}$. With these values, $R_0 = 1.99$. Since $\gamma_A = \gamma_C$, by Corollary 1, the endemic equilibrium is globally asymptotically stable.

7. Local sensitivity analysis

In this section, a local sensitivity analysis is carried out in order to identify which parameters have the greatest influence on changes in the values of R_0. Following the idea used in [38], let λ be any of the nine non-negative parameters: $\mu_h, N_h, \beta_h, \eta, \sigma, \gamma_C, \gamma_A, \beta_v$ and N_v that determine R_0.
If a small perturbation $\delta\lambda$ is made to the parameter λ, a corresponding change in R_0 will occur as δR_0, where:

$$\begin{aligned}\delta R_0 &= R_0(\lambda + \delta\lambda) - R_0(\lambda)\\ &\approx \delta\lambda \cdot \frac{\partial R_0}{\partial \lambda}.\end{aligned}$$

The normalized sensitivity index Ψ_λ is the ratio of the corresponding normalized changes, and is defined as

$$\Psi_\lambda = \frac{\frac{\partial R_0}{R_0}}{\frac{\partial \lambda}{\lambda}} = \frac{\lambda}{R_0}\frac{\partial R_0}{\partial \lambda}. \tag{7.1}$$

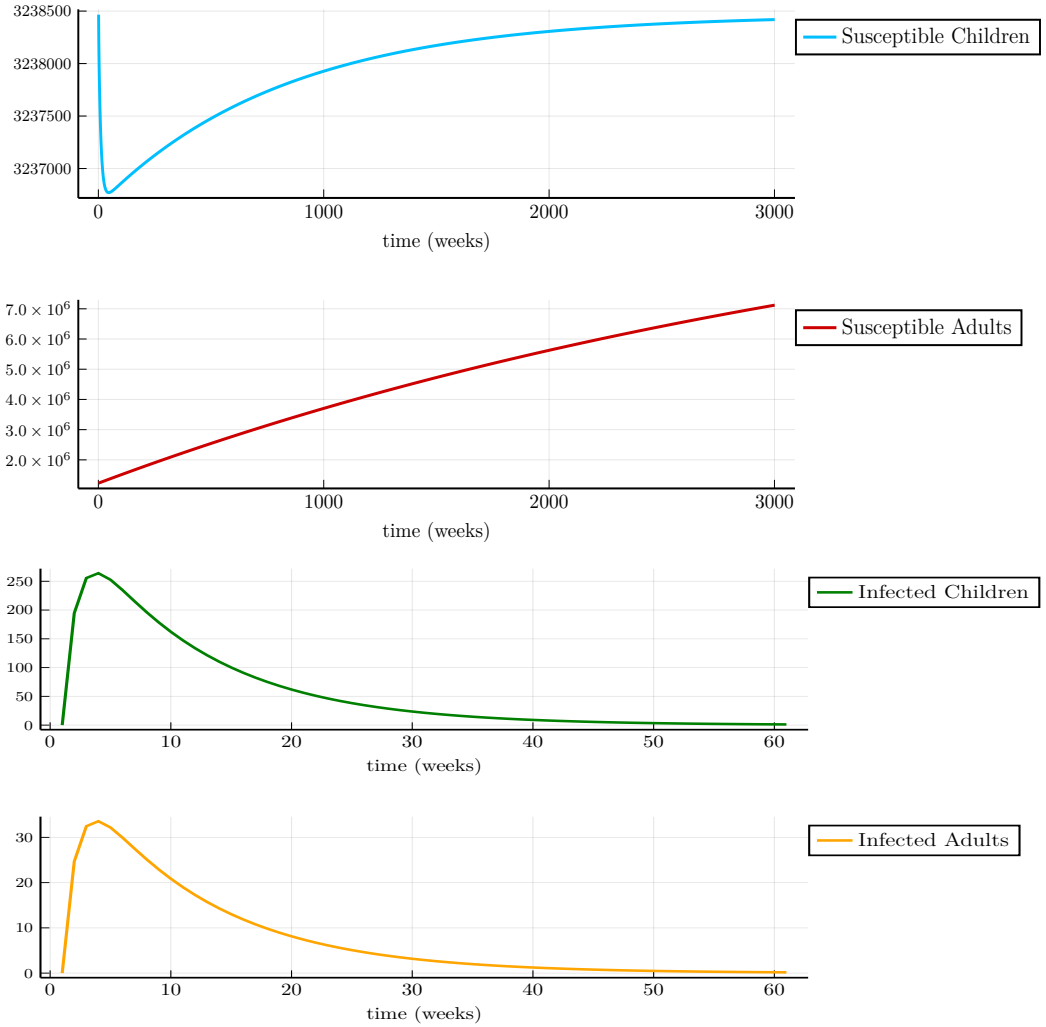

Figure 2. The trajectories of S_C, S_A, I_C and I_A toward the disease-free equilibrium. For $R_0 < 1$ (a) Susceptible children and adults; (b) Infected children and adults.

The normalized sensitivity indices for each of the parameters are given by the following expressions:

$$\Psi_{N_V} = \Psi_{\beta_h} = \Psi_{\beta_v} = 1,$$
$$\Psi_{N_h} = \Psi_{\mu_v} = -1.$$

We show that the normalized sensitivity indices of $\Psi_{N_h}, \Psi_{N_V}, \Psi_{\beta_h}, \Psi_{\beta_v}$ and Ψ_{μ_v} are constant, therefore they do not vary with respect to the value of the other parameters. On the other hand, the normalized sensitivity indices of $\Psi_{\mu_h}, \Psi_{\eta}, \Psi_{\sigma}, \Psi_{\gamma_C}$ and Ψ_{γ_A} depend on the other parameters.

$$\Psi_{\mu_h} = -\frac{\mu_h}{\eta+\mu_h}\left\{1+\frac{\beta_h\beta_v N_V}{\mu_v N_h R_0}\left[\frac{\eta\sigma^2}{(\gamma_A+\mu_h)^2}-\frac{\gamma_C}{(\gamma_C+\mu_h)^2}\right]\right\},$$
$$\Psi_{\eta} = \frac{\eta}{\eta+\mu}\left[\frac{1}{R_0}\frac{\sigma^2\beta_h\beta_v N_V}{\mu_v N_h(\gamma_A+\mu_h)}-1\right],$$

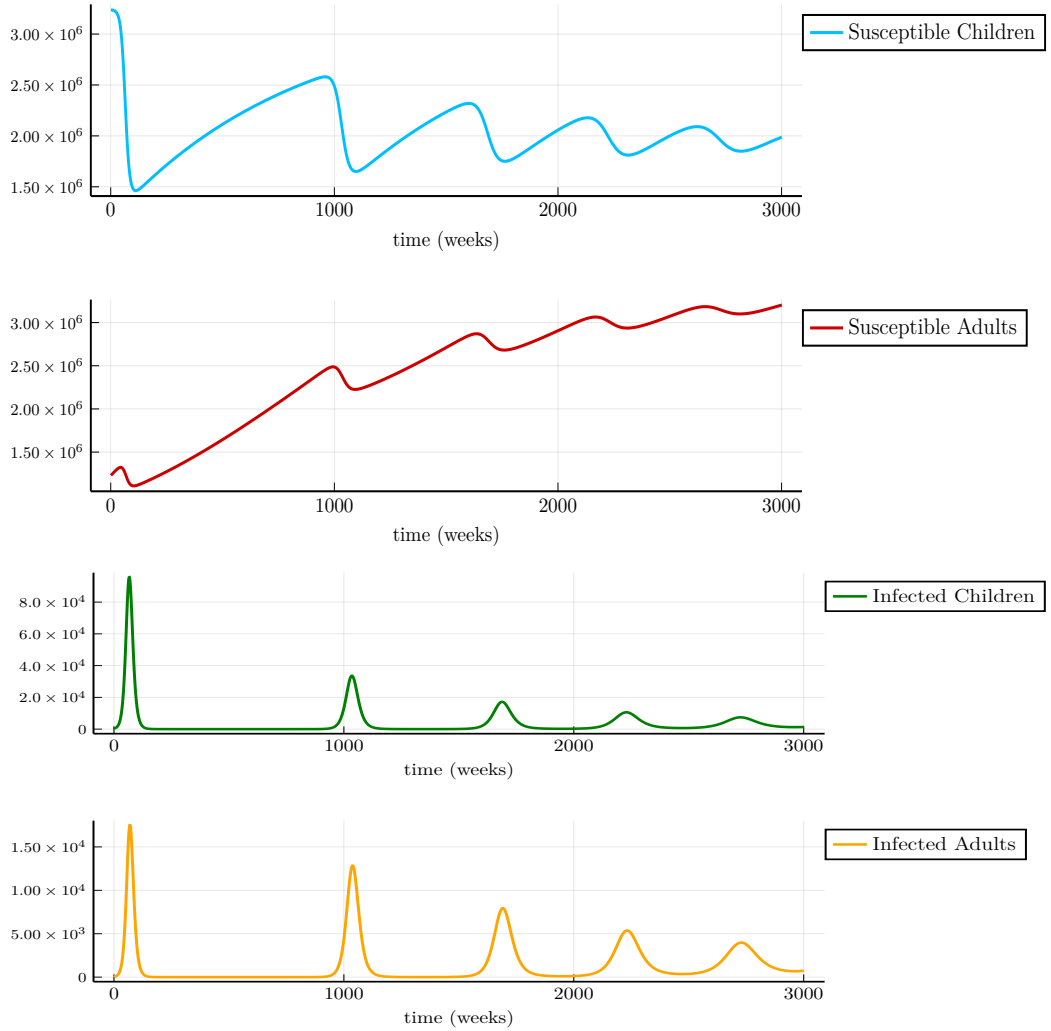

Figure 3. The trajectories of S_C, S_A, I_C and I_A toward the endemic equilibrium. For $R_0 > 1$ (a) Susceptible children and adults; (b) Infected children and adults.

$$\Psi_\sigma = \frac{2}{R_0}\frac{\eta\sigma^2\beta_h\beta_v N_V}{\mu_v N_h(\gamma_A+\mu_h)(\eta+\mu_h)},$$
$$\Psi_{\gamma_C} = -\frac{\gamma_C}{R_0}\frac{\mu_h\beta_h\beta_v N_V}{\mu_v N_h(\gamma_C+\mu_h)^2(\eta+\mu_h)},$$
$$\Psi_{\gamma_A} = -\frac{\gamma_A}{R_0}\frac{\eta\sigma^2\beta_h\beta_v N_V}{\mu_v N_h(\gamma_A+\mu_h)^2(\eta+\mu_h)}.$$

Using the parameters of the numerical simulations when $R_0 > 1$, we created Figure 4 and identified the influence of the parameters on the value of R_0.

The sensitivity indices shown in this figure indicate that the parameters N_V, β_h and β_v have perfect direct relationships with R_0. This indicates that increasing (or decreasing) by 1% the value of the parameters will produce an increase (or decrease) by 1% of the value of R_0. The index of the parameter N_h and μ_v have a perfect inverse relationships with R_0. This indicates that if we increase the value of

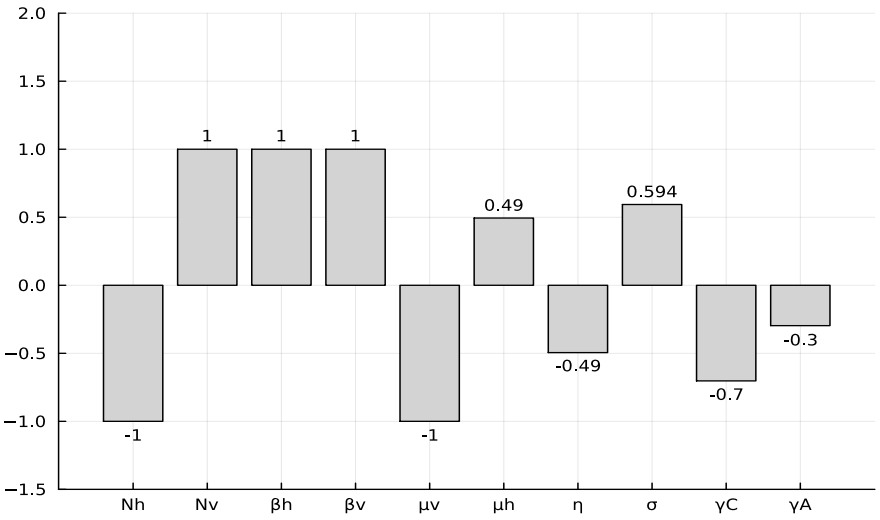

Figure 4. Sensitivity indices for R_0 with respect to the model parameters (2.2).

the parameter N_h and μ_v by 1%, then the value of R_0 will decrease by 1%. The parameters μ_h and η have the same magnitude of influence on R_0 but in the opposite direction. If we increase (or decrease) the value of the parameter μ_h by 10%, then the value of R_0 will increase (or decrease) by 4.9%, while if we increase the value of η by 10%, then the value of R_0 will decrease by 4.9%. For the parameter σ, the normalized sensitivity index indicates that if its value is increased (or decreased) by 10%, then the value of R_0 will increase (or decrease) by 5.9%. For the parameters γ_C and γ_A, an increase by 10% in their values will decrease the value of R_0 by 7% and 3% respectively.

8. Concluding remarks

In this paper, a mathematical model of the host–vector type was proposed. It considers the human population to be divided into two subpopulations: children and adults. This is in order to take into consideration that children are more likely to be bitten by mosquitoes than are adults.

A qualitative analysis of the model was carried out, obtaining two equilibria: a disease-free equilibrium E_0 and an endemic equilibrium E^*. It can be concluded that the stability of the equilibrium is completely determined by the value of R_0. If $R_0 < 1$, then the disease-free equilibrium is locally and globally asymptotically stable by Theorems 4.1 and 4.2, respectively. When $R_0 > 1$, then the disease-free equilibrium is unstable by Theorems 4.1 and an endemic equilibrium emerges in the interior of Ω. A sufficient condition (5.1) for the global stability of the endemic equilibrium was obtained in Theorem 5.1. We can interpret this condition as follows: the average residence time $1/(\gamma_C + \mu_h)$ in the class of infected children is greater than or equal to the product of the relative risk of being bitten by a mosquito (σ) and the average residence time $1/(\gamma_A + \mu_h)$ in the class of infected adults. On the other hand, assuming that $\gamma_C = \gamma_A$, we obtained Corollary 1 without sufficient conditions on parameters for the global asymptotic stability of the endemic equilibrium.

Numerical simulations were carried out for the value of the parameters of the model (2.2) to observe the behavior of its solutions in the scenarios when $R_0 < 1$ and when $R_0 > 1$. Figure 1 shows that dengue

will die out from the mosquito and human populations for any initial condition when $R_0 < 1$. Figure 2 shows that dengue remains present in the mosquito and human populations and will become endemic when $R_0 > 1$. Particularly, several outbreaks occur over a period of three thousand weeks, but each outbreak will have a lower number of cases than the previous one.

We observed that the relative risk (σ) of being bitten by a mosquito is quadratic in the basic reproductive number ($\hat{R}_0$), and σ is less than unity. The above explains the lesser contribution of adults compared to children to the dynamics of dengue transmission; this can be seen in the simulations presented in Figure 2 (b).

A sensitivity analysis can provide insights into possible strategies for the control of an epidemic. The results of the local sensitivity analysis (Figure 4) should be considered together with simulated outputs of epidemiological models for the possible interventions to be carried out. In our two-stage-structure model for dengue, the transmission rates (β_v and β_h) could be reduced by the use of anti-mosquito repellents or bed nets. Reducing the vector population (N_V) has been a classic control strategy and one of the measures with the greatest impact on vector-borne diseases. The vector mortality rate (μ_v) is traditionally increased by chemical, physical, and biological agents. The recovery rates (γ_C and γ_A) could be increased by developing antiviral therapies, which is still under investigation [39]. We note that the recovery rate of children γ_C has a greater influence on R_0 than does the recovery rate of adults γ_A. The sensitivity analysis allowed us to determine that the relative risk of being bitten by a mosquito σ has a greater influence on R_0 than do the recovery rates. So it is necessary to reduce the risks of children to mosquito bites when they spend time outdoors, maintaining self-protection such as the use of insect repellents. A systematic review conducted by Lima et al. [40] reports that the most effective control method was the integrated approach, considering the influence of eco-bio-social determinants in the virus–mosquito–human epidemiological chain, and community involvement. Several authors [40, 41] have pointed out that is important to engage and educate the community as active agents of vector control, apart from achieving the implementation of integrated approach.

Finally, we believe that children's increased risk of being bitten by mosquitoes is a fact that should be incorporated into age-group dengue models, given that vaccination strategies are focusing on children.

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Conflict of interest

The authors declare there is no conflict of interest.

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