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Stability analysis of five-grade Leishmania epidemic model with harmonic mean-type incidence rate

Karim Khan¹, Rahat Zarin², Amir Khan³, Abdullahi Yusuf^{4,5*} , Mohammed Al-Shomrani^{6*} and Arif Ullah¹

*Correspondence:

yusufabdullahi@fud.edu.ng;
malshamrani@kau.edu.sa

⁴Department of Computer Engineering, Biruni University, Istanbul, Turkey

⁶Department of Mathematics, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia

Full list of author information is available at the end of the article

Abstract

In this paper, we discuss the Anthroponotic Cutaneous Leishmania transmission. In addition, we develop a mathematical model for the Anthroponotic Cutaneous Leishmania transmission and consider its qualitative behavior. We derive the threshold number R_0 of the model using the next generation method. In the disease-free case, we carry out the local and global stability under the condition $R_0 < 1$. Moreover, we derive the global stability at the disease-free equilibrium point by utilizing the Castillo-Chavez method. On the other hand, at the endemic equilibrium point, we show the local and global stability to be held under specific conditions and $R_0 > 1$. We also establish the global stability at the endemic equilibrium point with the help of a geometrical approach, which is a generalization of Lyapunov theory, by using a second additive compound matrix. Finally, we take into account the sensitivity analysis of the threshold number with other parameters. We also discuss several graphs of important parameters.

Keywords: Compound matrix; Sensitivity analysis; Geometric approach; Stability analysis

1 Introduction

Leishmaniasis is the sixth most common disease affecting public health worldwide. It is a vector borne disease transmitted among mammalian hosts by the female sand fly. Most common animals carrying the Leishmania parasite are rodents, dogs, cattles, and foxes, this parasite primarily affecting the skin. Leishmaniasis cannot be transmitted from person to person through touch, blood transfusion, congenitally from mother to baby, infected needles and syringes, and so on. Different lab tests are performed to diagnose this parasite; for example, blood test for antibodies against the parasite, urine tests, and polymerase chain reaction (PCR) test can identify parasite based on its genetic fingerprint, and smear test identifies the parasite through a microscope.

The transmission of parasites is carried out by the species of genera *Phelobotomus* type. The sand flies are the main transmitter of these parasites. The habitat of these flies enjoys a wide range, from desert to tropical rain forest. Not only these but also several hosts in which dogs, chickens, humans, mammals, livestock, and vertebrates are considered to be

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the main hosts [1]. The color of these sand flies is sandy, and normally they are 2–3-mm long. The latent period of this sand fly is considered to be between three and seven days [2]. From the ground level, the sandflies attain 2.51 m (8.3 ft) as their maximum height [3]. The incidental transference risk of blood-borne pathogens of humans is reduced by the use of animal blood and is considered to be cheaper than the conservation of animals and their preparation for feeding sandfly [4]. The fecundity of species is badly affected by the extreme temperatures [5]. Some recent studies on Cutaneous Leishmaniasis epidemic models are described in [6–12]. Mathematical modeling is one of powerful tools to describe the dynamical behavior of different diseases [13–18].

Grouping and grading: Computational modeling of Leishmaniasis is developed to verify the prevalence and clearance of diseases in an endemic region. Patients are divided into two groups based on the disease grading. Group one includes patients from grades I–III, and group two includes grades IV–V. Grading of CL lesions is categorized on the basis of their clinical presentations. Specifically, the size (i.e., mean diameter) and shape of each CL lesion are assessed and subsequently used to classify the lesions on a numeric scale, from grade 1 (i.e., papule with mild overlying fine scales of size ≤ 1 cm), grade 2 (≤ 1 cm) nodule formation, grade 3 (< 2 cm) vesicle formation or ulceration, grade 4 (2–4 cm) vesicle formation and ulceration with rolled edges, and grade 5 (> 4 cm) vesicle formation, ulceration, and superadded infection.

1.1 Types of leishmaniasis

I. Mucocutaneous Leishmaniasis (MCL) is a less common form of Leishmaniasis, which is the partial or complete destruction of mucous membranes in the nose, throat, or mouth. It is either CL skin lesion to mucosa membrane or carried by direct bite of a sand fly on mucus membranes.

II. Visceral Leishmaniasis (VL) is the most lethal disease, which appears from days to year after a bite of an infected sand fly. This disease affects the internal organ like the liver, spleen, and bone marrow. Patients are symptomatically present with enlargement of the spleen and liver, weight loss, and episodes of fever. In Pakistan, both MCL and VL are rare.

III. Cutaneous Leishmaniasis (CL) is an ulcer appearance on the skin, which is usually developed in a couple of days after a bite of the sand fly. If the immunity of the patient is strong enough, then mostly these sores may heal spontaneously within a few days. According to the World Health Organization (WHO), 1–1.5 million new cases of CL are reported every year worldwide. Pakistan is one of the countries where the incident of CL is increasing yearly, and its main reason is poverty, negligible planning for vector control, inadequate medical facilities, armed conflicts, and mass migration of humans and cattle.

1.2 Treatment methods

Standard drugs: Meglumine antimoniate and sodium stibogluconate are used as a first-line conventional treatment worldwide to treat CL. These drugs are used oral and injectable. Besides their hard administration, it offers many side effects, and drugs are costly as well.

Conventional treatment: Some conventional domestic methods help in healing in CL wound: applying garlic water on the lesion, cleaning wound repeatedly with antiseptics, and placing a hot stone on wound have been reported by people.

Photodynamic therapy: Photodynamic therapy (PDT), the use of light of specific wavelength and energy, is a rapidly evolving therapeutic option for the treatment of CL. The

FDA has approved indications of PDT for various skin diseases, actinic keratosis, basal cell carcinoma, superficial squamous cell carcinoma, psoriasis, acne vulgaris, and sarcoidosis, verruca Vulgaris, and condyloma acuminatum. Treatment protocols of PDT are easy, patients’ comfort and lesion response to PDT make this the best option to treat CL.

Treatment protocols: Herein we present a number of cases of CL lesions at different sites of the body treated with PDT from Pakistan. These lesions had been diagnosed clinically as cutaneous Leishmaniasis (CL). The patients had received treatment (i.e., pentavalent antimoniate) with no satisfactory outcome. Clinical assessment showed that the patients had developed resistance to pentavalent antimoniate. The patients were planned for photodynamic therapy (PDT). Written and informed consent was obtained from the patient. To perform PDT, the lesions and the adjacent skin were cleaned and scrubbed to remove the necrotic layer and exudates dried up. The photosensitizer, methyl aminolevulinate (MAL), was applied locally on the lesions under an adhesive covering, followed by an incubation period of 3 hours for the absorption of the photosensitizer. After the incubation period, the cream was removed, and the lesion was washed with normal saline. The lesion was irradiated with red laser light (wavelength 635 nm); a light energy dose of 75 J/cm² was delivered as per the institutional protocol. The patient received three sessions of PDT; the first two sessions were repeated at two weeks intervals, whereas the third session was given at one-month intervals. The patient showed a complete response to PDT, being followed up regularly, and has remained disease-free for over two years.

2 Model formulation

Mathematical modeling of epidemic diseases has been widely studied by researchers [19–21]. The model is a modified version of Khan et al. [22], in which the total population $N(t)$ is partitioned into the following subpopulations. These classes are classified into four human population subclasses $S_h(t)$, $E_h(t)$, $I_{1h}(t)$, $I_{2h}(t)$, and $R_h(t)$, denoting the susceptible, exposed, infected people from grades I–III, infected people in grades IV and V, and recovered people. The three vector population subclasses $S_v(t)$, $E_v(t)$, and $I_v(t)$ represent susceptible, exposed, and infected vectors; the total human population is represented by $N_h(t) = S_h(t) + E_h(t) + I_{1h}(t) + I_{2h}(t) + R_h(t)$. Total total vector population is $N_v(t) = S_v(t) + E_v(t) + I_v(t)$.

The model is given as follows:

$$\begin{cases} \frac{dS_h}{dt} = \Gamma_h - \frac{2abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - \mu_h S_h(t), \\ \frac{dE_h}{dt} = \frac{2abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - (k_1 + \theta + \mu_h)E_h(t), \\ \frac{dI_{1h}}{dt} = k_1 E_h(t) - (\beta + \mu_h + k_2)I_{1h}(t), \\ \frac{dI_{2h}}{dt} = k_2 I_{1h}(t) - (\mu_h + \theta_1)I_{2h}(t), \\ \frac{dR_h}{dt} = \theta E_h(t) + \beta I_{1h}(t) + \theta_1 I_{2h}(t) - \mu_h R_h(t), \\ \frac{dS_v}{dt} = \Gamma_v - acI_{1h}(t)S_v(t) - adI_{2h}(t)S_v(t) - \mu_v S_v(t), \\ \frac{dE_v}{dt} = acI_{1h}(t)S_v(t) + adI_{2h}(t)S_v(t) - (\mu_v + k_3)E_v(t), \\ \frac{dI_v}{dt} = k_3 E_v(t) - \mu_v I_v(t), \end{cases} \tag{1}$$

with

$$S_h(t), E_h(t), I_{1h}(t), I_{2h}(t), R_h(t), S_v(t), E_v(t), I_v(t) \geq 0. \tag{2}$$

2.1 Basic properties of the model

The total-population dynamics is represented by

$$\frac{dN_h(t)}{dt} = \Gamma_h - \mu_h N_h(t), \tag{3}$$

$$\frac{dN_v(t)}{dt} = \Gamma_v - \mu_v N_v(t). \tag{4}$$

The feasible region (biological) Δ is

$$\Delta = \left\{ (S_h, E_h, I_{1h}, I_{2h}, R_h, S_v, E_v, I_v) \in \mathbb{R}_+^8, N_v \leq \frac{\Gamma_v}{\mu_v}; N_h \leq \frac{\Gamma_h}{\mu_h} \right\}. \tag{5}$$

From Eqs. (2) and (3) we obtain

$$N_h \rightarrow \frac{\Gamma_h}{\mu_h}, \quad N_v \rightarrow \frac{\Gamma_v}{\mu_v} \quad \text{as } t \rightarrow \infty, \tag{6}$$

which shows that the model is well posed and Δ is a positively invariant domain.

Lemma 1 *The orthant R_+^7 is invariant positively for system (1).*

Proof Let $X = (S_h, E_h, I_{1h}, I_{2h}, R_h, S_v, E_v, I_v)^T$ and assume that $a_{11} = \mu_h + \frac{2ab(I_v)^2}{(S_h+I_v)^2}$, $a_{21} = \frac{2abI_v^2}{(S_h+I_v)^2}$, $a_{22} = (k_1 + \theta + \mu_h)$, $a_{18} = \frac{-2ab(S_h)^2}{(S_h+I_v)^2}$, $a_{28} = \frac{-2ab(S_h)^2}{(S_h+I_v)^2}$, $a_{66} = acI_{1h} + adI_{2h} + \mu_v$, and $a_{76} = acI_{1h} + adI_{2h}$.

System (1) is expressed in the form

$$\frac{dX}{dt} = LX + B, \tag{7}$$

where

$$L = \begin{pmatrix} -a_{11} & 0 & 0 & 0 & 0 & 0 & 0 & a_{18} \\ a_{21} & -a_{22} & 0 & 0 & 0 & 0 & 0 & a_{28} \\ 0 & k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -(\theta_1 + \mu_h) & 0 & 0 & 0 & 0 \\ 0 & \theta & \beta & \theta_1 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & -acS_v & -adS_v & 0 & -a_{66} & 0 & 0 \\ 0 & 0 & acS_v & adS_v & 0 & a_{76} & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}, \tag{8}$$

$$B = \begin{pmatrix} 2abS_h - 2abS_h \\ 0 \\ 0 \\ 0 \\ 2acS_v - 2acS_v \\ 0 \\ 0 \end{pmatrix}. \tag{9}$$

Here we see that L is the Metzler matrix as it has nonnegative entries on its off-diagonal and $B \geq 0$. Hence we conclude that system (1) is positively invariant in R_+^8 . \square

Lemma 2 *If solutions of system (1) exist, then they are positive under the initial conditions (2) for all $t > 0$.*

Proof Let us assume that the solutions exist in I for all $t \in I \subset [0, \infty)$. Consider the second equation of (1). Its solution has the following form:

$$E_h(t) = E_h(0) \exp\{-(k_1 + \theta + \mu_h)t\} + \exp\{-(k_1 + \theta + \mu_h)t\} \times \int_0^t \frac{2abI_v(x)S_h(x)}{S_h(x) + I_v(x)} \exp\{(k_1 + \theta + \mu_h)x\} dx. \tag{10}$$

We also take the third equation, and its solution has the following form:

$$I_{1h}(t) = I_{1h}(0) \exp\{-(\beta + k_2 + \mu_h)t\} + \exp\{-(\beta + k_2 + \mu_h)t\} \times \int_0^t k_1 E_h(y) \exp\{(\beta + k_2 + \mu_h)y\} dy. \tag{11}$$

We can clearly see from the above solutions that these are strictly positive. In the same fashion, we can show that $S_h, R_h, S_v, E_v, I_{2h}$, and I_v possess nonnegative solutions. \square

2.2 Basic reproductive number R_0

The disease-free equilibrium point of system (1) is

$$E^0 = (S_h^0, E_h^0, I_{1h}^0, I_{2h}^0, R_h^0, S_v^0, E_v^0, I_v^0) = \left(\frac{\Gamma_h}{\mu_h}, 0, 0, 0, 0, \frac{\Gamma_v}{\mu_v}, 0, 0 \right). \tag{12}$$

Let $(E_h, I_{1h}, I_{2h}, E_v, I_v)$ be our infected compartment. Then from system (1) we have:

$$\begin{cases} \frac{dE_h}{dt} = \frac{2abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - (k_1 + \theta + \mu_h)E_h(t), \\ \frac{dI_{1h}}{dt} = k_1E_h(t) - (\beta + \mu_h + k_2)I_{1h}(t), \\ \frac{dI_{2h}}{dt} = k_2I_{1h}(t) - (\mu_h + \theta_1)I_{2h}(t), \\ \frac{dE_v}{dt} = acI_{1h}(t)S_v(t) + adI_{2h}(t)S_v(t) - (\mu_v + k_3)E_v(t), \\ \frac{dI_v}{dt} = k_3E_v(t) - \mu_vI_v(t). \end{cases} \tag{13}$$

Using the next generation matrix approach [23, 24], the Jacobian matrix J for this system at the disease-free equilibrium point is given by

$$J(E^0) = \begin{pmatrix} -(k_1 + \theta + \mu_h) & 0 & 0 & 0 & 2ab \\ k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 \\ 0 & k_2 & -(\mu_h + \theta_1) & 0 & 0 \\ 0 & \frac{ac\Gamma_v}{\mu_v} & \frac{ad\Gamma_v}{\mu_v} & -(\mu_v + k_3) & 0 \\ 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}.$$

Now decomposing the matrix J in terms of F and V as $J = F - V$, we get

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 2ab \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{ac\Gamma_v}{\mu_v} & \frac{ad\Gamma_v}{\mu_v} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$-V = \begin{pmatrix} (k_1 + \theta + \mu_h) & 0 & 0 & 0 & 0 \\ -k_1 & (\beta + k_2 + \mu_h) & 0 & 0 & 0 \\ 0 & -k_2 & (\mu_h + \theta_1) & 0 & 0 \\ 0 & 0 & 0 & (\mu_v + k_3) & 0 \\ 0 & 0 & 0 & -k_3 & \mu_v \end{pmatrix},$$

and

$$-V^{-1} = \begin{pmatrix} \frac{1}{(k_1 + \theta + \mu_h)} & 0 & 0 & 0 & 0 \\ \frac{k_2}{(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)} & \frac{1}{(\beta + k_2 + \mu_h)} & 0 & 0 & 0 \\ \frac{k_2^2}{(\beta + k_2 + \mu_h)(\theta + k_1 + \mu_h)(\mu_h + \theta_1)} & \frac{k_2}{(\mu_h + \theta_1)(k_2 + \beta + \mu_h)} & \frac{1}{\mu_h + \theta_1} & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{(\mu_v + k_3)} & 0 \\ 0 & 0 & 0 & \frac{1}{k_3\mu_v + \mu_v^2} & \frac{1}{\mu_v} \end{pmatrix}.$$

Now

$$-FV^{-1} = \begin{pmatrix} 0 & 0 & 0 & \frac{2ab}{\mu_v(\mu_v + k_3)} & \frac{2ab}{\mu_v} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \bar{A} & \bar{B} & \frac{ad\Gamma_v}{\mu_v(\mu_h + \theta_1)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where

$$\begin{cases} \bar{A} = \frac{ac\Gamma_vk_2}{\mu_v(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)} + \frac{ad\Gamma_vk_2^2}{\mu_v(\beta + k_2 + \mu_h)(\theta + k_1 + \mu_h)(\mu_h + \theta_1)}, \\ \bar{B} = \frac{ac\Gamma_v}{\mu_v(\beta + k_2 + \mu_h)} + \frac{ad\Gamma_vk_2}{\mu_v(\mu_h + \theta_1)(\beta + k_2 + \mu_h)}. \end{cases} \tag{14}$$

The characteristics equation of $[-FV^{-1}]$ becomes

$$-\lambda^3 \left(\lambda^2 - \bar{A} \frac{2ab}{\mu_v(k_3 + \mu_v)} \right) = 0. \tag{15}$$

The dominant eigenvalue gives us R_0 , that is,

$$\text{basic reproduction number} = \sqrt{\left(\frac{2a^2b\Gamma_vk_2(c(\mu_h + \theta_1) + dk_2)}{\mu_v^2(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)(\mu_v + k_3)(\mu_h + \theta_1)} \right)}.$$

3 Local stability

In this section, we establish the local stability of system (1) in this section at the disease-free point E^0 and endemic equilibrium point E^* .

3.1 Geometric interpretation of stability

For the DFE, the local stability implies that if there is a small perturbation of the system (e.g., a small number of infected individuals is introduced into the population), then after some time, the system will return to the DFE. However, a big perturbation may be able to drive the system to a different behavior, for example, convergence to the EE. If the stability of the DFE is global, then no matter the size of the perturbation, the disease will not be able to persist in the population.

On the other hand, the local stability of an equilibrium point means that if you put the system somewhere nearby the point, then it will move itself to the equilibrium point in some time. The global stability means that the system will come to the equilibrium point from any possible starting point (i.e., there is no “nearby” condition). Even in more physical interpretation, it could be like this: If DFE or EE is locally stable, then all epidemiological situations not-so-much different from the given stable equilibrium will (with time) evolve to (or transform into) the equilibrium point. Also, this means that the equilibria are stable to small perturbations: if you push the situation a bit out from the equilibrium point, then the situation will return back on its own (from the physicist’s point of view, this means that the equilibrium may be a stable situation in real life because the real world always is somewhat noisy). The global stability of an equilibrium point in this case maybe described as “the inevitable fate of the epidemic process regardless of its starting situation”. However, a caveat should be put that this “inevitability” holds as long as the world strictly follows the underlying mathematical model of the epidemic process. For still even more lay (or medical) audience, all these things may be easily interpreted in terms of “adding or removing a small number of infectious people”, but we believe it would make the central idea less clear.

3.2 At disease free equilibrium point

Theorem 3.1 *System (1) at disease-free equilibrium point E^0 is locally asymptotically stable if $R_0 < 1$.*

Proof For system (1), the Jacobian matrix at E^0 is given by

$$J^{[0]} = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & 0 & -2ab \\ 0 & -(k_1 + \theta + \mu_h) & 0 & 0 & 0 & 0 & 0 & 2ab \\ 0 & k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -(\mu_h + \theta_1) & 0 & 0 & 0 & 0 \\ 0 & \theta & \beta & \theta_1 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & -\frac{ac\Gamma_v}{\mu_v} & -\frac{ad\Gamma_v}{\mu_v} & 0 & -\mu_v & 0 & 0 \\ 0 & 0 & \frac{ac\Gamma_v}{\mu_v} & \frac{ad\Gamma_v}{\mu_v} & 0 & 0 & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}.$$

We can clearly see that three eigenvalues are negative, namely, $\lambda_1 = -\mu_h$, $\lambda_2 = -\mu_h$, and $\lambda_3 = -\mu_v$. For the rest of eigenvalues, we consider the following reduced matrix:

$$J_1^{[0]} = \begin{pmatrix} -(k_1 + \theta + \mu_h) & 0 & 0 & 0 & 2ab \\ k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 \\ 0 & k_2 & -(\mu_h + \theta_1) & 0 & 0 \\ 0 & \frac{ac\Gamma_v}{\mu_v} & \frac{ad\Gamma_v}{\mu_v} & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}.$$

After simplification, we get:

$$J_2^{[0]} = \begin{pmatrix} -L_{11} & 0 & 0 & 0 & 2ab \\ 0 & -L_{22} & 0 & 0 & 2abk_1 \\ 0 & 0 & -L_{33} & 0 & 2abk_1k_2 \\ 0 & 0 & 0 & -L_{44} & L_{45} \\ 0 & 0 & 0 & 0 & -L_{55} \end{pmatrix},$$

$$L_{11} = (k_1 + \theta + \mu_h), \quad L_{22} = (k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h),$$

$$L_{33} = (k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h)(\theta_1 + \mu_h),$$

$$L_{44} = (k_1 + \theta + \mu_h)^2(k_2 + \beta + \mu_h)^2(\theta_1 + \mu_h)(\mu_v + k_2),$$

$$L_{55} = \frac{2abk_1k_2k_3ad\Gamma_v}{\mu_v}(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h) + \frac{2abk_1k_2ac\Gamma_v}{\mu_v}L_{33} - \mu_v(\mu_v + k_2)L_{33}L_{22},$$

$$L_{45} = \frac{2abk_1k_2ad\Gamma_v}{\mu_v}(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h) + \frac{2abk_1ac\Gamma_v}{\mu_v}L_{33}.$$

The eigenvalues of $J_2^{[0]}$ take the following form:

$$\lambda_4 = -(k_1 + \theta + \mu_h) < 0, \quad \lambda_5 = -(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h) < 0,$$

$$\lambda_6 = -(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h)(\theta_1 + \mu_h) < 0,$$

$$\lambda_7 = -(k_1 + \theta + \mu_h)^2(k_2 + \beta + \mu_h)^2(\theta_1 + \mu_h)(\mu_v + k_2) < 0,$$

and

$$\lambda_8 = \frac{2abk_1k_2k_3ad\Gamma_v}{\mu_v}(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h) + \frac{2abk_1k_2ac\Gamma_v}{\mu_v}(k_1 + \theta + \mu_h)(k_2 + \beta + \mu_h)(\theta_1 + \mu_h) - \mu_v(\mu_v + k_2)(k_1 + \theta + \mu_h)^2(k_2 + \beta + \mu_h)^2(\theta_1 + \mu_h) < 0.$$

The last eigenvalue also has the negative real part since

$$\left(\frac{2a^2b\Gamma_vk_2(c(\mu_h + \theta_1) + dk_2)}{\mu_v^2(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)(\mu_v + k_3)(\mu_h + \theta_1)} \right) < 1$$

implies that

$$\sqrt{\left(\frac{2a^2b\Gamma_vk_2(c(\mu_h + \theta_1) + dk_2)}{\mu_v^2(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)(\mu_v + k_3)(\mu_h + \theta_1)} \right)} < 1.$$

Thus under the condition $R_0 < 1$, the real part of all eigenvalues are negative. Hence, for $R_0 < 1$, system (1) is locally asymptotically stable. \square

3.3 At endemic equilibrium point

We rearrange system (1) to get $S_h^*, E_h^*, I_{2h}^*, R_h^*, S_v^*, E_v^*$, and I_v^* in terms of I_{1h}^* :

$$\begin{cases} S_h^* = \frac{\Gamma_h k_1 - (k_1 + \theta + \mu_h)(\beta + k_2 + \mu_h) I_{1h}^*}{k_1 \mu_h}, \\ S_v^* = \frac{\Gamma_v (\theta_1 + \mu_h)}{(ac(\theta_1 + \mu_h) - adk_2) I_{1h}^* + \mu_v (\theta_1 + \mu_h)}, \\ I_{2h}^* = \frac{k_1 I_{1h}^*}{(\theta_1 + \mu_h)}, \quad E_h^* = \frac{(k_2 + \beta + \mu_h) I_{1h}^*}{k_1}, \\ E_v^* = \frac{(ac(\theta_1 + \mu_h) + adk_2) I_{1h}^* S_v^*}{(\mu_v + k_3)(\theta_1 + \mu_h)}, \quad I_v^* = \frac{k_3 E_v^*}{\mu_v}, \\ R_h^* = \frac{(\theta(\theta_1 + \mu_h)(\beta + k_2 + \mu_h) + \beta k_1(\theta_1 + \mu_h) + k_1 k_2 \theta_1) I_{1h}^*}{\mu_h k_1 (\theta_1 + \mu_h)}. \end{cases} \tag{16}$$

Theorem 3.2 *If $R_0 \in (1, \sqrt{\frac{(S_h^* + I_h^*)^2 + 2abI_v^*}{(\mu_v + \theta_1)S_h^{*2}}})$, then the endemic equilibrium E^* of system (1) is locally asymptotically stable.*

Proof. For system (1), the Jacobian matrix at E^* is given by

$$J^{*|} = \begin{pmatrix} -a_{11} & 0 & 0 & 0 & 0 & 0 & 0 & \frac{-2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \\ \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} & -a_{22} & 0 & 0 & 0 & 0 & 0 & \frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \\ 0 & k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -(\theta_1 + \mu_h) & 0 & 0 & 0 & 0 \\ 0 & \theta & \beta & \theta_1 & -\mu_h & 0 & 0 & 0 \\ 0 & 0 & -acS_v^* & -adS_v^* & 0 & -a_{66} & 0 & 0 \\ 0 & 0 & acS_v^* & adS_v^* & 0 & a_{76} & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}, \tag{17}$$

where $a_{11} = \mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2}$, $a_{22} = (k_1 + \theta + \mu_h)$, $a_{66} = acI_{1h}^* + adI_{2h}^* + \mu_v$, and $a_{76} = acI_{1h}^* + adI_{2h}^*$.

Clearly, one eigenvalue of the Jacobian matrix $J^{*|}$ of model (1) around the disease present equilibrium point E^* is negative, that is, $\lambda_1 = -\mu_h < 0$. For the remaining seven eigenvalues, we take the following reduced matrix:

$$J_1^{*|} = \begin{pmatrix} -a_{11} & 0 & 0 & 0 & 0 & 0 & \frac{-2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \\ \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} & -a_{22} & 0 & 0 & 0 & 0 & \frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \\ 0 & k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 & 0 \\ 0 & 0 & k_2 & -(\theta_1 + \mu_h) & 0 & 0 & 0 \\ 0 & 0 & -acS_v^* & -adS_v^* & -a_{66} & 0 & 0 \\ 0 & 0 & acS_v^* & adS_v^* & a_{76} & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix}. \tag{18}$$

After simplification we get:

$$J_2^{*|} = \begin{pmatrix} -Z_{11} & 0 & 0 & 0 & 0 & 0 & -\Lambda \\ 0 & -Z_{22} & 0 & 0 & 0 & 0 & \Lambda_1 \\ 0 & 0 & -Z_{33} & 0 & 0 & 0 & \Lambda_1 k_1 \\ 0 & 0 & 0 & -Z_{44} & 0 & 0 & \Lambda_1 k_1 k_2 \\ 0 & 0 & 0 & 0 & -Z_{55} & -(\mu_v + k_2) & 0 \\ 0 & 0 & 0 & 0 & 0 & -Z_{66} & \Lambda_2 \\ 0 & 0 & 0 & 0 & 0 & 0 & -Z_{77} \end{pmatrix}, \tag{19}$$

where

$$\begin{aligned} Z_{11} &= \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right), Z_{22} = (k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right), \\ Z_{33} &= (\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right), \\ Z_{44} &= (\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) (\theta_1 + \mu_h), \quad Z_{55} = \mu_v, \\ Z_{66} &= (\mu_v + k_2)(\beta + k_2 + \mu_h)^2 (k_1 + \theta + \mu_h)^2 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right)^2 \\ &\quad \times [acI_{1h}^* + adI_{1h}^* + (\mu_v + k_2)], \\ Z_{77} &= \left(k_3(\mu_v + k_2)(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)k_1 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) \right) \left[\mu_h \frac{2ac(I_h^*)^2}{(S_v^* + I_h^*)^2} \right] \\ &\quad - \mu_v(\mu_v + k_2)(\beta + k_2 + \mu_h)^2 (k_1 + \theta + \mu_h)^2 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right)^2 \\ &\quad \times [acI_{1h}^* + adI_{1h}^* + (\mu_v + k_2)], \\ \Lambda &= -\frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2}, \quad \Lambda_1 = \frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) - \frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2}, \\ \Lambda_2 &= \left((\mu_v + k_2)(\beta + k_2 + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) (k_1 + \theta + \mu_h)k_1 \frac{2ab(S_h^*)^2}{(S_h^* + I_v^*)^2} \right) \\ &\quad \times \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) [acS_v^* + adS_v^*]. \end{aligned}$$

The eigenvalues of $J_2^{*|}$ take the following forms:

$$\begin{aligned} \lambda_2 &= -\left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) < 0, \quad \lambda_3 = -(k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) < 0, \\ \lambda_4 &= -(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) < 0, \\ \lambda_5 &= -(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h) \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) (\theta_1 + \mu_h), \quad \lambda_6 = -\mu_v, \end{aligned}$$

$$\lambda_7 = -(\mu_v + k_3)(\beta + k_2 + \mu_h)^2(k_1 + \theta + \mu_h)^2 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right)^2 \times [acI_{1h}^* + adI_{1h}^* + (\mu_v + k_3)] < 0,$$

and

$$\lambda_8 = \left(k_3(\mu_v + k_3)(\beta + k_2 + \mu_h)(k_1 + \theta + \mu_h)k_1 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right) \right) \left[\mu_h \frac{2ac(I_h^*)^2}{(S_v^* + I_h^*)^2} \right] - \mu_v(\mu_v + k_2)(\beta + k_2 + \mu_h)^2(k_1 + \theta + \mu_h)^2 \left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \right)^2 \times [acI_{1h}^* + adI_{1h}^* + (\mu_v + k_3)] < 0$$

iff $1 < R_0 < \sqrt{\left(\frac{(S_h^* + I_h^*)^2 + 2abI_v^*}{(\mu_v + \theta_1)S_h^{*2}} \right)}$.

4 Global asymptotic stability

Here we discuss the global stability analysis of model (1) for both disease-free and endemic equilibria. We use the method of Castillo-Chavez et al. [25] to establish the global stability for disease-free equilibrium, whereas for the global stability of endemic equilibrium, we use the generalization of Lyapunov theory [26].

4.1 At disease-free equilibrium point

For model (1), the global stability at the disease-free point is achieved by taking into account the Castillo-Chavez approach [25]. The method is summarized by the reduction of the proposed model (1) to the following two subsystems:

$$\begin{aligned} \frac{d\chi_1}{dt} &= G(\chi_1, \chi_2), \\ \frac{d\chi_2}{dt} &= H(\chi_1, \chi_2). \end{aligned} \tag{20}$$

In system (20), χ_1 and χ_2 represent the numbers of uninfected and infected individuals, respectively, that is, $\chi_1 = (S_h, S_v, R_h) \in R^3$ and $\chi_2 = (I_{1h}, I_{2h}, I_v, E_h, E_v) \in R^4$. The disease-free equilibrium is denoted by E^0 and defines as $E^0 = (\chi_1^0, 0)$. Thus the existence of the global stability at the disease-free equilibrium point depends on the following two conditions:

1. If $\frac{d\chi_1}{dt} = G(\chi_1, 0)$, then χ_1^0 is globally asymptotically stable.
2. $H(\chi_1, \chi_2) = B\chi_2 - \bar{H}(\chi_1, \chi_2)$, where $\bar{H}(\chi_1, \chi_2) \geq 0$ for $(\chi_1, \chi_2) \in \Delta$.

At the second condition, $B = D_{\chi_2}H(\chi_1^0, 0)$ is an M -matrix with positive off-diagonal entries, and Δ is the feasible region.

Lemma 3 ([25]) *For $R_0 < 1$, the equilibrium point $E^0 = (\chi_1^0, 0)$ of system (1) is globally asymptotically stable if the above conditions are satisfied.*

Theorem 4.1 *If $R_0 < 1$, then the proposed model (1) is globally asymptotically stable at the disease-free equilibrium E^0 and unstable otherwise.*

Proof Let $\chi_1 = (S_h, S_v, R_h)$ and $\chi_2 = (I_{1h}, I_{2h}, I_v, E_h, E_v)$, and define $E^0 = (\chi_1^0, 0)$, where

$$\chi_1^0 = \left(\frac{\Gamma_h}{\mu_h}, \frac{\Gamma_v}{\mu_v} \right). \tag{21}$$

By using model system (1) we have

$$\begin{aligned} \frac{d\chi_1}{dt} &= G(\chi_1, \chi_2), \\ \frac{d\chi_2}{dt} &= \begin{pmatrix} \Gamma_h - \frac{2abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - \mu_h S_h(t) \\ \theta E_h(t) + \beta I_{1h}(t) + \theta_1 I_{2h}(t) - \mu_h R_h(t) \\ \Gamma_v - acI_{1h}(t)S_v(t) - adI_{2h}(t)S_v(t) - \mu_v S_v(t) \end{pmatrix}. \end{aligned} \tag{22}$$

For $S_h = S_h^0, S_v = S_v^0$, and $G(\chi_1, 0) = 0$, we get

$$G(\chi_1, 0) = \begin{pmatrix} \Gamma_h - \mu_h S_h \\ \Gamma_v - \mu_v S_v \end{pmatrix}. \tag{23}$$

Thus from equation (23) we have that $\chi_1 \rightarrow \chi_1^0$ as $t \rightarrow \infty$. So $\chi_1 = \chi_1^0$ is globally asymptotically stable.

Now

$$\begin{aligned} B\chi_2 - \bar{H}(\chi_1, \chi_2) &= \begin{pmatrix} -(k_1 + \theta + \mu_h) & 0 & 0 & 0 & 2ab \\ k_1 & -(\beta + k_2 + \mu_h) & 0 & 0 & 0 \\ 0 & k_2 & -(\mu_h + \theta_1) & 0 & 0 \\ 0 & acS_v^0 & adS_v^0 & -(\mu_v + k_3) & 0 \\ 0 & 0 & 0 & k_3 & -\mu_v \end{pmatrix} \begin{pmatrix} E_h \\ I_{1h} \\ I_{2h} \\ E_v \\ I_v \end{pmatrix} \\ &\quad - \begin{pmatrix} 2ab - \frac{2abI_v S_h}{S_h + I_v} \\ 0 \\ 0 \\ acS_v^0 + adS_v^0 - (acI_{1h}S_v + adI_{2h}S_v) \\ 0 \end{pmatrix}. \end{aligned} \tag{24}$$

As the total population is bounded by S_h^0 and S_v^0 , that is $S_h \leq S_h^0$ and $S_v \leq S_v^0$, so $2ab \geq \frac{2abI_v S_h}{S_h + I_v}$ and $acS_v^0 + adS_v^0 \geq (acI_{1h}S_v + adI_{2h}S_v)$, which implies that $\bar{H}(\chi_1, \chi_2) \geq 0$. Clearly, B is an M -matrix, and hence both the conditions are proved, so by Lemma 1 the disease-free equilibrium point E^0 is stable globally asymptotically. \square

4.2 Endemic equilibrium (global stability)

“For the global stability of (1) at the endemic equilibrium E^* , we use the geometrical approach [26]. Thus we investigate the sufficient condition through which the E^* is globally asymptotically stable. Therefore consider the differential equation

$$\dot{x} = f(x), \tag{25}$$

where the open set $U \subset \mathbb{R}^n$ is simply connected, and $f : U \rightarrow \mathbb{R}^n$ is a function such that $f \in C^1(U)$. Assuming that $f(x^*) = 0$ is the solution of equation (25), for $x(t, x_0)$, the following are true:

3. There exist a compact absorbing set $K \in U$.
4. System (25) has a unique equilibrium.

The solution x^* is said to be globally asymptotically stable in U if it is locally asymptotically stable and all trajectories in U converge to the equilibrium x^* . For $n \geq 2$, a condition satisfied for f , which precludes the existence of nonconstant periodic solution of equation (25), is known as the Bendixson criterion. The classical Bendixson criterion $\text{div}f(x) < 0$ for $n = 2$ is robust under C^1 [26]. Furthermore, a point $x_0 \in U$ is wandering for equation (25) if there exist a neighborhood N of x_0 and $\tau > 0$ such that $N \cap x(t, N)$ is empty for all $t > \tau$. Thus the following global stability principle established for autonomous system in any finite dimension.

Lemma 4 *If the conditions (3)–(4) and Bendixson criterion are satisfied for equation (25) (i.e., robust under C^1 local perturbation of f at all nonequilibrium nonwandering point for equation (25)), then x^* is globally asymptotically stable in U , provided that it is stable.*

Define a matrix-valued function P on U by

$$P(x) = \begin{pmatrix} n \\ 1 \end{pmatrix} \times \begin{pmatrix} n \\ 1 \end{pmatrix}. \tag{26}$$

Further, assume that P^{-1} exists and is continuous for $x \in K$. Now define the quantity

$$\bar{q} = \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t [\mu(B(x(s, x_0)))] ds, \tag{27}$$

where $J^{[2]}$ is the second additive compound matrix of J , that is, $J(x) = Uf(x)$ and $B = P_f P^{-1} + P J^{[2]} P^{-1}$. Let $\ell(B)$ be the Lozinski measure of the matrix B with respect to the norm $\|\cdot\|$ in \mathbb{R}^n [27] defined by

$$\ell(B) = \lim_{x \rightarrow 0} \frac{|I + Bx| - 1}{x}. \tag{28}$$

Hence if $\bar{q} < 0$, then the presence of any orbit gives rise to a simple closed rectifiable curve such as a periodic orbit and heterocyclic cycle.

Lemma 5 *Let U be simply connected, and let conditions (3)–(4) be satisfied. Then the unique equilibrium x^* of equation (25) is globally asymptotically stable in U if $\bar{q} < 0$.*

Now we apply the above techniques to prove the global stability of model (1) at the endemic equilibrium. We have the following stability.

Theorem 4.2 *If $\frac{2b(I_v^*)^2}{(S_h^* + I_v^*)^2} > \frac{E_h(cI_h^* + dI_{2h}^*)}{S_h}$, $(cI_{1h}^* + dI_{2h}^*) > \frac{2bE_v(I_v^*)^2}{S_v(S_h^* + I_v^*)^2}$, and $R_0 > 1$, then model (29) is globally asymptotically stable at the endemic equilibrium E^* and unstable otherwise.*

Proof To prove the global asymptotic stability of the proposed model (1) at the endemic equilibrium E^* , let us consider the subsystem of (1)

$$\begin{cases} \frac{dS_h}{dt} = \Gamma_h - ab\left(\frac{2I_v(t)S_h(t)}{S_h(t)+I_v(t)}\right) - \mu_h S_h(t), \\ \frac{dE_h}{dt} = ab\left(\frac{2I_v(t)S_h(t)}{S_h(t)+I_v(t)}\right) - (k_1 + \theta + \mu_h)E_h(t), \\ \frac{dS_v}{dt} = \Gamma_v - acI_{1h}(t)S_v(t) - adI_{2h}(t)S_v(t) - \mu_v S_v(t), \\ \frac{dE_v}{dt} = acI_{1h}(t)S_v(t) + adI_{2h}(t)S_v(t) - (\mu_v + k_3)E_v(t). \end{cases} \tag{29}$$

Let us start with the Jacobian matrix of system (29)

$$J = \begin{pmatrix} j_{11} & j_{12} & j_{13} & j_{14} \\ j_{21} & j_{22} & j_{23} & j_{24} \\ j_{31} & j_{32} & j_{33} & j_{34} \\ j_{41} & j_{42} & j_{43} & j_{44} \end{pmatrix}.$$

The third additive compound matrix is given by

$$J^{[3]} = \begin{pmatrix} j_{11} + j_{22} + j_{33} & j_{34} & -j_{24} & j_{14} \\ j_{43} & j_{11} + j_{22} + j_{44} & j_{23} & -j_{13} \\ -j_{42} & j_{32} & j_{11} + j_{33} + j_{44} & j_{12} \\ j_{41} & -j_{31} & j_{21} & j_{22} + j_{33} + j_{44} \end{pmatrix}. \tag{30}$$

Let J be the Jacobian matrix of system (29) given by

$$J = \begin{pmatrix} -\left(\mu_h + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2}\right) & 0 & 0 & 0 \\ \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} & -(k_1 + \theta + \mu_h) & 0 & 0 \\ 0 & 0 & -(\mu_v + acI_{1h}^* + adI_{2h}^*) & 0 \\ 0 & 0 & (acI_{1h}^* + adI_{2h}^*) & -(\mu_v + k_3) \end{pmatrix}.$$

The third additive compound matrix of J is denoted by $J^{[3]}$ and defined as

$$J^{[3]} = \begin{pmatrix} A_{11} & 0 & 0 & 0 \\ (acI_{1h}^* + adI_{2h}^*) & A_{22} & 0 & 0 \\ 0 & 0 & A_{33} & 0 \\ 0 & 0 & \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} & A_{44} \end{pmatrix}, \tag{31}$$

where

$$\begin{aligned} A_{11} &= j_{11} + j_{22} + j_{33} \\ &= -\left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + k_1 + \theta + 2\mu_h + \mu_v + acI_{1h}^* + adI_{2h}^*\right), \\ A_{22} &= j_{11} + j_{22} + j_{44} \\ &= -\left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \mu_v + k_3 + k_1 + \theta + 2\mu_h\right), \end{aligned}$$

$$\begin{aligned}
 A_{33} &= j_{11} + j_{33} + j_{44} \\
 &= -\left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \mu_h + acI_{1h}^* + adI_{2h}^* + 2\mu_v + k_3 \right), \\
 A_{44} &= j_{22} + j_{33} + j_{44} \\
 &= -(k + \theta + \mu_h + acI_{1h}^* + adI_{2h}^* + 2\mu_v + k_3).
 \end{aligned}$$

Let us choose a function $p(\chi) = p(S_h, E_h, S_v, E_v)$ so that $p(\chi) = \text{diag}\{S_h, E_h, S_v, E_v\}$, which implies that $p^{-1}(\chi) = \text{diag}\{\frac{1}{S_h}, \frac{1}{E_h}, \frac{1}{S_v}, \frac{1}{E_v}\}$. The time derivative of $p(\chi)$ yields that $P_f(\chi) = \text{diag}\{\dot{S}_h, \dot{E}_h, \dot{S}_v, \dot{E}_v\}$.

A direct computation shows that $B = P_f P^{-1} + P J^{[3]} P^{-1}$, which becomes

$$\begin{aligned}
 P_f P^{-1} &= \text{diag} \left\{ \frac{\dot{S}_h}{S_v}, \frac{\dot{E}_h}{E_h}, \frac{\dot{S}_v}{S_v}, \frac{\dot{E}_v}{E_v} \right\}, \\
 P J^{[3]} P^{-1} &= \begin{pmatrix} A_{11} & 0 & 0 & 0 \\ \frac{E_h}{S_h}(acI_{1h}^* + adI_{2h}^*) & A_{22} & 0 & 0 \\ 0 & 0 & A_{33} & 0 \\ 0 & 0 & \frac{2ab(I_v^*)^2 E_v}{(S_h^* + I_v^*)^2 S_v} & A_{44} \end{pmatrix}, \tag{32}
 \end{aligned}$$

so that $B = P_f P^{-1} + P J^{[3]} P^{-1}$,

$$B = \begin{pmatrix} a_{11} & 0 & 0 & 0 \\ a_{21} & a_{22} & 0 & 0 \\ 0 & 0 & a_{33} & 0 \\ 0 & 0 & a_{43} & a_{44} \end{pmatrix}, \tag{33}$$

where

$$\begin{aligned}
 a_{11} &= \frac{\dot{S}_h}{S_h} - \left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + k_1 + \theta + 2\mu_h + \mu_v + acI_{1h}^* + adI_{2h}^* \right), \\
 a_{21} &= \frac{E_h}{S_h}(acI_{1h}^* + adI_{2h}^*), \quad a_{22} = \frac{\dot{E}_h}{E_h} - \left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \mu_v + k_3 + k_1 + \theta + 2\mu_h \right), \\
 a_{43} &= \frac{2ab(I_v^*)^2 E_v}{(S_h^* + I_v^*)^2 S_v}, \quad a_{33} = \frac{\dot{S}_v}{S_v} - \left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \mu_h + acI_{1h}^* + adI_{2h}^* + 2\mu_v + k_3 \right), \\
 a_{44} &= \frac{\dot{E}_v}{E_v} - (k_1 + \theta + \mu_h + acI_{1h}^* + adI_{2h}^* + 2\mu_v + k_3).
 \end{aligned}$$

Consequently,

$$\begin{aligned}
 h_1(t) &= a_{11} + \sum_{j=2}^4 |a_{1j}|, \\
 h_1(t) &= \frac{\dot{S}_h}{S_h} - \left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + k_1 + \theta + 2\mu_h + \mu_v + acI_{1h}^* + adI_{2h}^* \right) \\
 &\leq \frac{\dot{S}_h}{S_h} - (2\mu_h + k_1 + \theta + \mu_v),
 \end{aligned}$$

and if $\frac{2b(I_v^*)^2}{(S_h^* + I_v^*)^2} > \frac{E_h(cI_{1h}^* + dI_{2h}^*)}{S_h}$, then

$$\begin{aligned}
 h_2(t) &= a_{22} + \sum_{j=1 \text{ and } j \neq 2}^4 |a_{2j}|, \\
 h_2(t) &= \frac{\dot{E}_h}{E_h} - (\mu_v + k_3 + k_1 + \theta + 2\mu_h) - \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \frac{E_h}{S_h} (acI_{1h}^* + adI_{2h}^*) \\
 &= \frac{\dot{E}_h}{E_h} - (\mu_v + k_3 + k_1 + \theta + 2\mu_h) - a \left(\frac{2b(I_v^*)^2}{(S_h^* + I_v^*)^2} - \frac{E_h(cI_{1h}^* + dI_{2h}^*)}{S_h} \right) \\
 &\leq \frac{\dot{E}_h}{E_h} - (\mu_v + k_3 + k_1 + \theta + 2\mu_h),
 \end{aligned}$$

Similarly,

$$\begin{aligned}
 h_3(t) &= a_{33} + \sum_{j=1 \text{ and } j \neq 3}^4 |a_{3j}|, \\
 h_3(t) &= \frac{\dot{S}_v}{S_v} - \left(\frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} + \mu_h + acI_{1h}^* + adI_{2h}^* + 2\mu_v + k_3 \right) \\
 &\leq \frac{\dot{S}_v}{S_v} - (\mu_h + 2\mu_v + k_3)
 \end{aligned}$$

and if $(cI_{1h}^* + dI_{2h}^*) > \frac{2bE_v(I_v^*)^2}{S_v(S_h^* + I_v^*)^2}$, then

$$\begin{aligned}
 h_4(t) &= a_{44} + \sum_{j=1}^3 |a_{4j}|, \\
 h_4(t) &= \frac{\dot{E}_v}{E_v} - (k_1 + \theta + \mu_h + 2\mu_v + k_3) - (acI_{1h}^* + adI_{2h}^*) + \frac{2ab(I_v^*)^2}{(S_h^* + I_v^*)^2} \frac{E_v}{S_v} \\
 &= \frac{\dot{E}_v}{E_v} - (k_1 + \theta + \mu_h + 2\mu_v + k_3) - a \left((cI_{1h}^* + dI_{2h}^*) - \frac{2bE_v(I_v^*)^2}{S_v(S_h^* + I_v^*)^2} \right) \\
 &\leq \frac{\dot{E}_v}{E_v} - (k_1 + \theta + \mu_h + 2\mu_v + k_3).
 \end{aligned}$$

Let (b_1, b_2, b_3, b_4) be a vector in \mathbf{R}^4 . The Lozinski measure $\mu(B)$ is defined as $\mu(B) = h_i$, $i = 1, 2, 3, 4$. The integration of the Lozinski measure $\mu(B)$ and taking the limits as $t \rightarrow \infty$ lead to the following equations:

$$\begin{aligned}
 \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t h_1(t) dt &\leq \frac{1}{t} \log \frac{S_h(t)}{S_h(0)} - (2\mu_h + k_1 + \theta + \mu_v) \\
 &< -(2\mu_h + k_1 + \theta + \mu_v), \\
 \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t h_2(t) dt &\leq \frac{1}{t} \log \frac{E_h(t)}{E_h(0)} - (\mu_h + \mu_v + k_3 + k_1 + \theta + \mu_h) \\
 &< -(2\mu_h + \mu_v + k_3 + k_1 + \theta),
 \end{aligned}$$

$$\begin{aligned} \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t h_3(t) dt &\leq \frac{1}{t} \log \frac{S_v(t)}{S_v(0)} - (\mu_h + 2\mu_v + k_3) \\ &< -(\mu_h + 2\mu_v + k_3), \\ \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t h_4(t) dt &\leq \frac{1}{t} \log \frac{E_v(t)}{E_v(0)} - (k_1 + \theta + \mu_h + 2\mu_v + k_3) \\ &< -(k_1 + \theta + \mu_h + 2\mu_v + k_3). \end{aligned}$$

Thus combining these four inequalities, we get the following equation:

$$\bar{q} = \limsup_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mu(B) dt < 0.$$

The system containing the first four equations of model (1) is globally asymptotically stable around its interior equilibrium $(S_h^*, E_h^*, S_v^*, E_v^*)$. Now consider the subsystem of model (1)

$$\begin{cases} \frac{dI_{1h}}{dt} = k_1 E_h(t) - (\beta + \mu_h + k_2) I_{1h}(t), \\ \frac{dI_{2h}}{dt} = k_2 I_{1h}(t) - (\mu_h + \theta_1) I_{2h}(t), \\ \frac{dR_h}{dt} = \theta E_h(t) + \beta I_{1h}(t) + \theta_1 I_{2h}(t) - \mu_h R_h(t), \\ \frac{dI_v}{dt} = k_3 E_v(t) - \mu_v I_v(t). \end{cases} \tag{34}$$

Now rewrite the system in the form

$$\begin{cases} \frac{dI_{1h}}{dt} + (\beta + \mu_h + k_2) I_{1h}(t) = k_1 E_h^*(t), \\ \frac{dI_{2h}}{dt} + (\mu_h + \theta_1) I_{2h}(t) = k_2 I_{1h}^*(t), \\ \frac{dR_h}{dt} + \mu_h R_h(t) = \theta E_h^*(t) + \beta I_{1h}^*(t) + \theta_1 I_{2h}^*(t), \\ \frac{dI_v}{dt} + \mu_v I_v(t) = k_3 E_v^*(t). \end{cases} \tag{35}$$

The integrating factors for the system are $e^{t(\beta+k_2+\mu_h)}$, $e^{t(\mu_h+\theta_1)}$, $e^{t(\mu_h)}$, and $e^{t(\mu_v)}$.

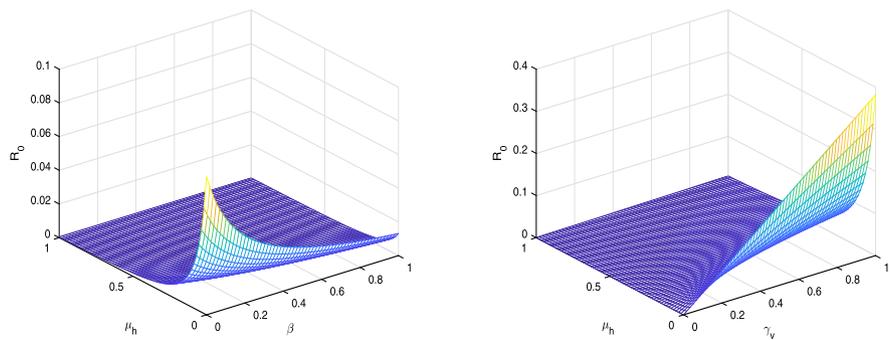
Using the integrating factors, we solve the system. So for large time t , that is, $t \rightarrow \infty$, $I_{1h} \rightarrow I_{1h}^*$, $I_{2h} \rightarrow I_{2h}^*$, $R_h \rightarrow R_h^*$, and $I_v \rightarrow I_v^*$, which means that the endemic equilibrium point E^* is globally asymptotically stable. \square

5 Sensitivity analysis

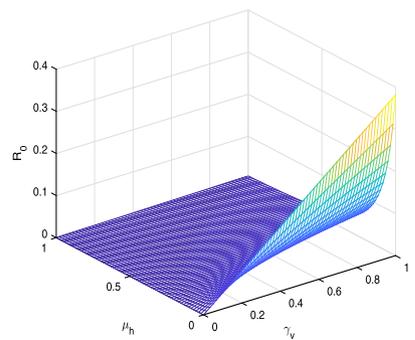
Determining the parameters that are helpful in decreasing the spread of infectious disease is carried out by sensitivity analysis. Forward sensitivity analysis is considered a vital component of disease modeling although its computation becomes tedious for complex biological models. Sensitivity analysis of R_0 has received much attention from the ecologists and epidemiologists. The behavior of the R_0 with some suitable values of the parameters are shown in Fig. 1.

Definition 1 The normalized forward sensitivity index of R_0 that depends differentiably on a parameter ω is defined as

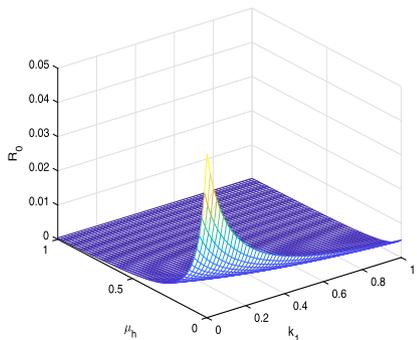
$$S_\omega = \frac{\omega}{R_0} \frac{\partial R_0}{\partial \omega}. \tag{36}$$



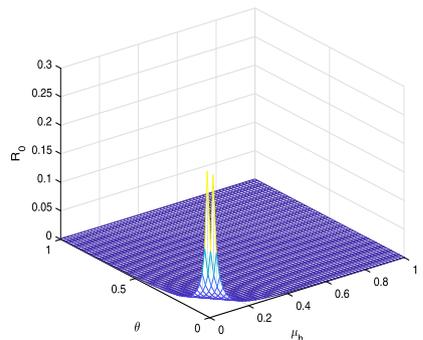
(a) R_0 versus sensitive parameters μ_h and β .



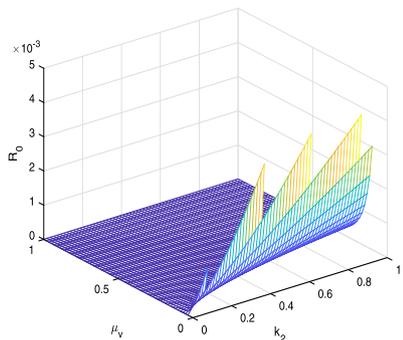
(b) R_0 versus sensitive parameters μ_h and γ_v .



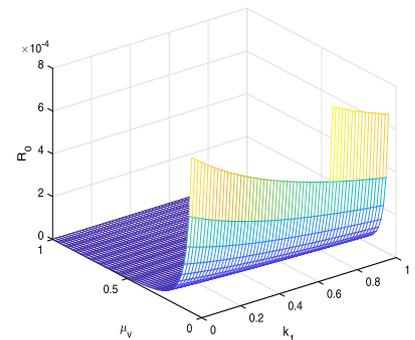
(c) R_0 versus sensitive parameters μ_h and k_1 .



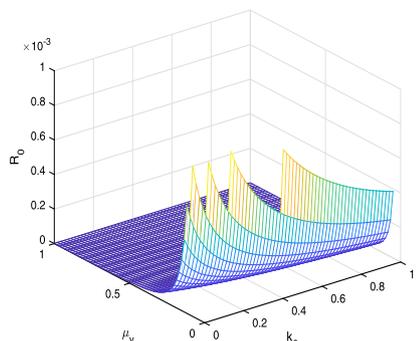
(d) R_0 versus sensitive parameters μ_h and θ .



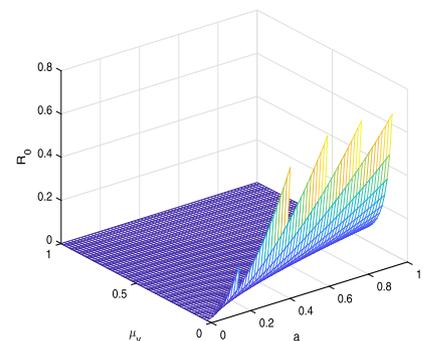
(e) R_0 versus sensitive parameters μ_v and k_2 .



(f) R_0 versus sensitive parameters μ_v and k_1 .



(g) R_0 versus sensitive parameters μ_v and k_3 .



(h) R_0 versus sensitive parameters μ_v and a .

Figure 1 Sensitivity analysis of different parameters

Table 1 Sensitivity indices of the reproduction number R_0 against mentioned parameters

Parameter	S. Index	Value	Parameter	S. Index	Value
a	S_a	1.000000000	b	S_b	0.4999999999
θ	S_θ	-0.004792332271	k_1	S_{k_1}	0.1006389778
c	S_c	0.5000000001	k_2	S_{k_2}	0.01754385961
μ_h	S_{μ_h}	-0.3685739184	μ_v	S_{μ_v}	-0.5175438600
β	S_β	-0.2272727272	Γ_h	S_{Γ_h}	0.0
Γ_v	S_{Γ_v}	0.0	θ_1	S_{θ_1}	0.0254635451
d	S_d	1.000000000	k_3	S_{k_3}	0.4999999999

Three methods are normally used to calculate the sensitivity indices: (i) by direct differentiation, (ii) by a Latin hypercube sampling method, and (iii) by linearizing system (1) and then solving the obtained set of linear algebraic equations. We will apply the direct differentiation method as it gives analytical expressions for the indices. The indices not only show us the influence of various aspects associated with the spreading of infectious disease but also gives us important information regarding the comparative change between R_0 and different parameters. Consequently, it helps in developing the control strategies. Table 1 shows that the parameters $a, b, k_1, c, k_2, \theta_1, d,$ and k_3 have a positive influence on the reproduction number R_0 ; for example, the growth or decay of these parameters, say, by 10% will increase or decrease the reproduction number by 10%, 4.9%, 1.0%, 5.0%, 0.17%, 0.25%, 10%, and 4.9%, respectively. On the other hand, the indices for parameters $\theta, \mu_h, \mu_v,$ and β illustrate that increasing their values by 10% will decrease the values of reproduction number R_0 by 0.04%, 3.6%, 5.1%, and 2.2%, respectively. Note that Γ_h and Γ_v have no impact on the reproduction number.

6 Optimal control

By using these control variables our control problem becomes

$$\left\{ \begin{aligned}
 \frac{dS_h}{dt} &= \Gamma_h - \frac{2(1-u_1(t))abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - \mu_h S_h(t), \\
 \frac{dE_h}{dt} &= \frac{2(1-u_1(t))abI_v(t)S_h(t)}{S_h(t)+I_v(t)} - (k_1 + \theta + \mu_h)E_h(t), \\
 \frac{dI_{1h}}{dt} &= k_1 E_h(t) - (u_2(t) + \beta + \mu_h + k_2)I_{1h}(t), \\
 \frac{dI_{2h}}{dt} &= k_2 I_{1h}(t) - (u_2(t) + \mu_h + \theta_1)I_{2h}(t), \\
 \frac{dR_h}{dt} &= \theta E_h(t) + (\beta + u_2(t))I_{1h}(t) + (\theta_1 + u_2(t))I_{2h}(t) - \mu_h R_h(t), \\
 \frac{dS_v}{dt} &= \Gamma_v - (1 - u_1(t))acI_{1h}(t)S_v(t) - (1 - u_1(t))adI_{2h}(t)S_v(t) \\
 &\quad - (u_3(t) + \mu_v)S_v(t), \\
 \frac{dE_v}{dt} &= (1 - u_1(t))acI_{1h}(t)S_v(t) + (1 - u_1(t))adI_{2h}(t)S_v(t) \\
 &\quad - (u_3(t) + \mu_v + k_3)E_v(t), \\
 \frac{dI_v}{dt} &= k_3 E_v(t) - (u_3(t) + \mu_v)I_v(t).
 \end{aligned} \right. \tag{37}$$

The goal of our optimal control strategies is minimizing the infectious and exposed human population, the vector population, sandfly biting rate, and the cost of implementing the control by using possible minimal control variables $u_1(t), u_2(t),$ and $u_3(t)$. To do this, we

use the bounded Lebesgue-measurable control to construct the objective functional

$$\begin{aligned}
 J(u_1, u_2, u_3) = & \int_0^1 \left(g_1 E_h(t) + g_2 I_{1h}(t) + g_3 I_{2h}(t) + g_4 (S_v(t) + E_v(t) + I_v(t)) \right. \\
 & \left. + \frac{1}{2} (d_1 u_1^2(t) + d_2 u_2^2(t) + d_3 u_3^2(t)) \right) dt \tag{38}
 \end{aligned}$$

subject to system (37).

In the objective functional, $g_1, g_2, g_3,$ and g_4 represent the weight constants of the exposed, infectious human, and of vector population, respectively, $d_1, d_2,$ and d_3 are weight constants of human self-protection, human treatment, and vector control, respectively. The terms $(1/2)d_1 u_1^2(t), (1/2)d_2 u_2^2(t),$ and $(1/2)d_3 u_3^2(t)$ describe the costs of disease interventions. The cost associated with the first control strategy $u_1(t)$ comes from the cost of sandfly repellent lotions, electric mats, and mosquito bed nets. The cost associated with the second control strategy $u_2(t)$ is the cost of expensive medication of human class. The cost associated with the third control strategy $u_3(t)$ can arise from applying different types chemical pesticides to kill sand flies at any stage of their life. We have assumed the costs as proportional to the square of the corresponding control function. We aim to find control functions such that

$$J(u_1^*, u_2^*, u_3^*) = \min \{ J(u_1, u_2, u_3), (u_1, u_2, u_3) \in D \}$$

subject to system (4). The control set D is defined as

$$D = \{ (u_1, u_2, u_3) \mid u_i(t) \text{ is Lebesgue measurable on } [0, 1], 0 \leq u_i(t) < 1, i = 1, 2, 3 \}.$$

6.1 Existence of the control problem

For the existence of the control problem, we consider the control system (37) with initial conditions at $t = 0$. In case of bounded Lebesgue-measurable controls and nonnegative initial conditions, there exists a nonnegative bounded solution of the state system [28, 29]. For optimal solution of the system, we first find the Lagrangian and Hamiltonian. We define the Lagrangian of the control problem (37) as

$$L(t) = g_1 E_h(t) + g_2 I_{1h}(t) + g_3 I_{2h}(t) + g_4 N_v(t) + \frac{1}{2} (d_1 u_1^2(t) + d_2 u_2^2(t) + d_3 u_3^2(t)), \tag{39}$$

where $N_v(t) = S_v(t) + E_v(t) + I_v(t)$.

We define the Hamiltonian H to find the minimal value of the Lagrangian as follows:

$$\begin{aligned}
 H(t) = & g_1 E_h(t) + g_2 I_{1h}(t) + g_3 I_{2h}(t) + g_4 N_v(t) + \frac{1}{2} [d_1 u_1^2(t) + d_2 u_2^2(t) + d_3 u_3^2(t)] \\
 & + \left[\lambda_1(t) \left(\Gamma_h - \frac{2(1 - u_1(t))abI_v(t)S_h(t)}{S_h(t) + I_v(t)} - \mu_h S_h(t) \right) \right] \\
 & + \left[\lambda_2(t) \left(\frac{2(1 - u_1(t))abI_v(t)S_h(t)}{S_h(t) + I_v(t)} - (k_1 + \theta + \mu_h)E_h(t) \right) \right] \\
 & + [\lambda_3(t)(k_1 E_h(t) - (u_2(t) + \beta + \mu_h + k_2)I_{1h}(t))] \\
 & + [\lambda_4(t)(k_2 I_{1h}(t) - (u_2(t) + \mu_h + \theta_1)I_{2h}(t))] \\
 & + [\lambda_5(t)(\theta E_h(t) + (\beta + u_2(t))I_{1h}(t) + (\theta_1 + u_2(t))I_{2h}(t) - \mu_h R_h(t))] \tag{40}
 \end{aligned}$$

$$\begin{aligned}
 &+ [\lambda_6(t)(\Gamma_v - (1 - u_1(t))acI_{1h}(t)S_v(t) - (1 - u_1(t))adI_{2h}(t)S_v(t) \\
 &- (u_3(t) + \mu_v)S_v(t))] \\
 &+ [\lambda_7(t)((1 - u_1(t))acI_{1h}(t)S_v(t) + (1 - u_1(t))adI_{2h}(t)S_v(t) \\
 &- (u_3(t) + \mu_v + k_3)E_v(t))] \\
 &+ [\lambda_8(t)(k_3E_v(t) - (u_3(t) + \mu_v)I_v(t))].
 \end{aligned}$$

Theorem 6.1 *There exists an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in D$ such that $J(u_1, u_2, u_3) = \min_{(u_1, u_2, u_3) \in D} J(u_1, u_2, u_3)$ subject to system (37) and initial conditions at $t = 0$.*

Proof The control variables and the state variables are nonnegative. So we use the result in [28, 29] for the existence of an optimal control. The necessary convexity of the objective functional in u_1, u_2 , and u_3 is satisfied here. Also, by definition the set of the control variables $(u_1, u_2, u_3) \in D$ is convex and closed. The compactness, which we need for the existence of an optimal control, is confirmed by the boundedness of the optimal system. Also, the integrand in the functional (38), $g_1E_h(t) + g_2I_{1h}(t) + g_3I_{2h}(t) + g_4N_v(t) + \frac{1}{2}(d_1u_1^2(t) + d_2u_2^2(t) + d_3u_3^2(t))$, is convex on the control set D . We can find a constant $\eta > 1$ and positive numbers ξ_1 and ξ_2 such that $J(u_1, u_2, u_3) \geq \xi_1(|u_1|^2, |u_2|^2, |u_3|^2)^{\frac{\eta}{2}} - \xi_2$, as the state variables are bounded. This completes the proof of the existence of an optimal control.

For optimal solution, we apply Pontryagin’s maximum principle [30] as follows. If $(x(t), u(t))$ is an optimal solution of an optimal control problem, then there exists a non-trivial vector function $\lambda(t) = (\lambda_1(t), \lambda_2(t), \dots, \lambda_n(t))$ satisfying the following:

$$\begin{aligned}
 \frac{dx(t)}{dt} &= \frac{\partial H(t, x, u, \lambda)}{\partial \lambda}, \\
 0 &= \frac{\partial H(t, x, u, \lambda)}{\partial u}, \\
 \lambda'(t) &= -\frac{\partial H(t, x, u, \lambda)}{\partial x}.
 \end{aligned}$$

We apply the necessary conditions to the Hamiltonian H in system (40). □

Theorem 6.2 *Let $S_h^*, E_h^*, I_h^*, R_h^*, S_v^*, E_v^*$, and I_v^* be optimal state solutions with associated optimal control variables (u_1^*, u_2^*, u_3^*) for the optimal control problem system (37)–(38). Then there exist adjoint variables $\lambda_i, i = 1, 2, \dots, 8$, satisfying*

$$\left\{ \begin{aligned}
 \frac{d\lambda_1(t)}{dt} &= \lambda_1(t) \frac{2(1-u_1(t))abI_v^{*2}(t)}{(S_h^*(t)+I_v^*(t))^2} - \lambda_2(t) \frac{2(1-u_1(t))abI_v^{*2}(t)}{(S_h^*(t)+I_v^*(t))^2} - \lambda_1(t)\mu_h, \\
 \frac{d\lambda_2(t)}{dt} &= \lambda_2(t)(k_1 + \theta + \mu_h) - \lambda_3(t)k_1 - \lambda_5(t)\theta - g_1, \\
 \frac{d\lambda_3(t)}{dt} &= (\lambda_6 - \lambda_7)(1 - u_1(t))acS_v^* - \lambda_4k_2 + \lambda_3(u_2(t) + \beta + \mu_h + k_2) \\
 &\quad - \lambda_5(\beta + u_2(t)) - g_2, \\
 \frac{d\lambda_4(t)}{dt} &= (\lambda_6 - \lambda_7)(1 - u_1(t))adS_v^* + \lambda_4(u_2(t) + \mu_h + \theta_1) - \lambda_5(\theta_1 + u_2(t)) - g_3, \\
 \frac{d\lambda_5(t)}{dt} &= \lambda_5\mu_h, \\
 \frac{d\lambda_6(t)}{dt} &= (\lambda_6 - \lambda_7)(1 - u_1(t))acI_{1h}^*(t) + (\lambda_6 - \lambda_7)(1 - u_1(t))adI_{2h}^*(t) \\
 &\quad + \lambda_6(u_3(t) + \mu_v) - g_4, \\
 \frac{d\lambda_7(t)}{dt} &= \lambda_7(u_3(t) + \mu_v + k_3) - \lambda_8k_3 - g_3, \\
 \frac{d\lambda_8(t)}{dt} &= \lambda_1(t) \frac{2(1-u_1(t))abS_h^{*2}(t)}{(S_h^*(t)+I_v^*(t))^2} - \lambda_2(t) \frac{2(1-u_1(t))abS_h^{*2}(t)}{(S_h^*(t)+I_v^*(t))^2} + (u_3(t) + \mu_v)\lambda_8 - g_4.
 \end{aligned} \right. \tag{41}$$

We have the transversality conditions

$$\lambda_i(T) = 0, \quad i = 1, 2, 3, \dots, 8, \tag{42}$$

for the control set u_i , and hence we have

$$\frac{\partial H}{\partial u_i} = 0, \quad i = 1, 2, 3.$$

By the optimality condition we have

$$\left. \frac{\partial H}{\partial u_1} \right|_{u_1=u_1^*} = 0,$$

that is,

$$\frac{\partial H}{\partial u_1} = d_1 u_1 + (\lambda_1 - \lambda_2) \frac{2abI_v^*(t)S_h^*(t)}{(S_h^*(t) + I_v^*(t))} + (\lambda_6 - \lambda_7)acI_{1h}^*(t)S_v^* + (\lambda_6 - \lambda_7)adI_{2h}^*(t)S_v^*.$$

Similarly,

$$\begin{aligned} \left. \frac{\partial H}{\partial u_1} \right|_{u_1=u_1^*} &= d_1 u_1^* + (\lambda_1 - \lambda_2) \frac{2abI_v^*(t)S_h^*(t)}{(S_h^*(t) + I_v^*(t))} + (\lambda_6 - \lambda_7)acI_{1h}^*(t)S_v^* \\ &\quad + (\lambda_6 - \lambda_7)adI_{2h}^*(t)S_v^* = 0, \end{aligned}$$

or

$$u_1^* = \frac{(\lambda_2 - \lambda_1) \frac{2abI_v^*(t)S_h^*(t)}{(S_h^*(t) + I_v^*(t))} + (\lambda_7 - \lambda_6)acI_{1h}^*(t)S_v^* + (\lambda_7 - \lambda_6)adI_{2h}^*(t)S_v^*}{d_1}.$$

Also,

$$\left. \frac{\partial H}{\partial u_2} \right|_{u_2=u_2^*} = 0,$$

that is,

$$\frac{\partial H}{\partial u_2} = d_2 u_2^* + (\lambda_5 - \lambda_3 I_{1h}^*) + (\lambda_5 - \lambda_4 I_{2h}^*) = 0,$$

or

$$u_2^* = \frac{(\lambda_3 - \lambda_5 I_{1h}^*) + (\lambda_4 - \lambda_5 I_{2h}^*)}{d_2},$$

and

$$\left. \frac{\partial H}{\partial u_3} \right|_{u_3=u_3^*} = 0,$$

that is,

$$\frac{\partial H}{\partial u_3} = d_3 u_3^* - \lambda_7 E_v^*(t) - \lambda_8 I_v^*(t) = 0,$$

or

$$u_3^* = \frac{\lambda_7 E_v^*(t) + \lambda_8 I_v^*(t)}{d_3}.$$

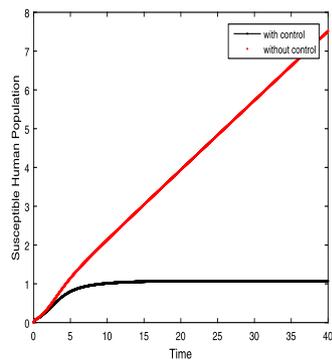
Now using an appropriate variation argument and taking the bounds into account, we obtain

$$\begin{aligned}
 u_1^*(t) &= \max \left\{ \min \left\{ \frac{(\lambda_2 - \lambda_1) \frac{2abI_v^*(t)S_h^*(t)}{(S_h^*(t)+I_v^*(t))} + (\lambda_7 - \lambda_6)acI_{1h}^*(t)S_v^* + (\lambda_7 - \lambda_6)adI_{2h}^*(t)S_v^*}{d_1}, 1 \right\}, 0 \right\}, \\
 u_2^*(t) &= \max \left\{ \min \left\{ \frac{(\lambda_3 - \lambda_5 I_{1h}^*) + (\lambda_4 - \lambda_5 I_{2h}^*)}{d_2}, 1 \right\}, 0 \right\}, \\
 u_3^*(t) &= \max \left\{ \min \left\{ \frac{\lambda_7 E_v^*(t) + \lambda_8 I_v^*(t)}{d_3}, 1 \right\}, 0 \right\}.
 \end{aligned} \tag{43}$$

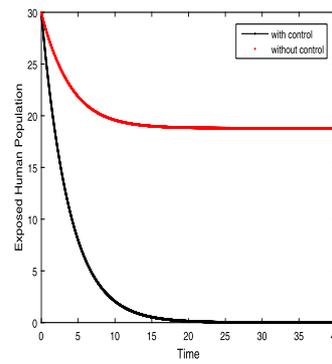
These are optimal, as required.

Proof To find adjoint equations and the transversality conditions, we use Eq. (37). Differentiating the Hamiltonian H with respect to each state variable, we obtain system (41). Solving the equations $\frac{\partial H}{\partial u_1} = 0$, $\frac{\partial H}{\partial u_2} = 0$, and $\frac{\partial H}{\partial u_3} = 0$ on the interior of the control set and using the optimality conditions and the property of the control space D , we derive Eqs. (43). The optimal control and the state are found by solving the optimality system (38), the adjoint system $\frac{d\lambda_i}{dt}$, initial and boundary conditions (42), and equations of the optimal control (43). Since the second derivatives of the Lagrangian with respect to u_1, u_2 , and u_3 are positive, the optimal problem is minimum at the controls u_1^*, u_2^* , and u_3^* . By substituting the values of u_1^*, u_2^* , and u_3^* into the control system (40) we get the following system:

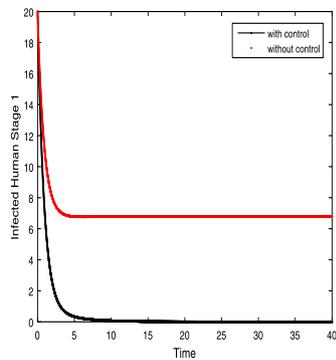
$$\begin{cases}
 \frac{dS_h^*}{dt} = \Gamma_h - \frac{2(1-u_1^*(t))abI_v^*(t)S_h^*(t)}{S_h^*(t)+I_v^*(t)} - \mu_h S_h^*(t), \\
 \frac{dE_h^*}{dt} = \frac{2(1-u_1^*(t))abI_v^*(t)S_h^*(t)}{S_h^*(t)+I_v^*(t)} - (k_1 + \theta + \mu_h)E_h^*(t), \\
 \frac{dI_{1h}^*}{dt} = k_1 E_h^*(t) - (u_2^*(t) + \beta + \mu_h + k_2)I_{1h}^*(t), \\
 \frac{dI_{2h}^*}{dt} = k_2 I_{1h}^*(t) - (u_2^*(t) + \mu_h + \theta_1)I_{2h}^*(t), \\
 \frac{dR_h^*}{dt} = \theta E_h^*(t) + (\beta + u_2^*(t))I_{1h}^*(t) + (\theta_1 + u_2^*(t))I_{2h}^*(t) - \mu_h R_h^*(t), \\
 \frac{dS_v^*}{dt} = \Gamma_v - (1 - u_1^*(t))acI_{1h}^*(t)S_v^*(t) - (1 - u_1^*(t))adI_{2h}^*(t)S_v^*(t) \\
 \quad - (u_3^*(t) + \mu_v)S_v^*(t), \\
 \frac{dE_v^*}{dt} = (1 - u_1^*(t))acI_{1h}^*(t)S_v^*(t) + (1 - u_1^*(t))adI_{2h}^*(t)S_v^*(t) \\
 \quad - (u_3^*(t) + \mu_v + k_3)E_v^*(t), \\
 \frac{dI_v^*}{dt} = k_3 E_v^*(t) - (u_3^*(t) + \mu_v)I_v^*(t),
 \end{cases} \tag{44}$$



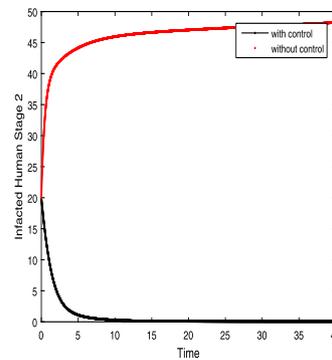
(a) The plot represents the susceptible individuals.



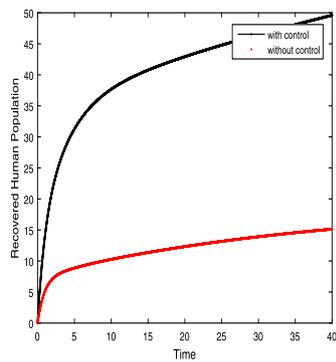
(b) The plot represents the exposed individuals.



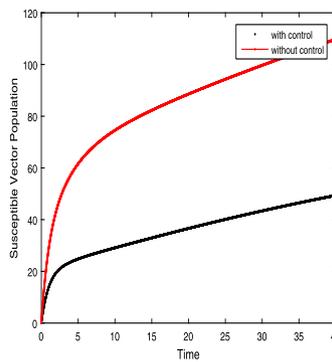
(c) The plot represents the infected individuals.



(d) The plot represents the infected individuals of stage 2.

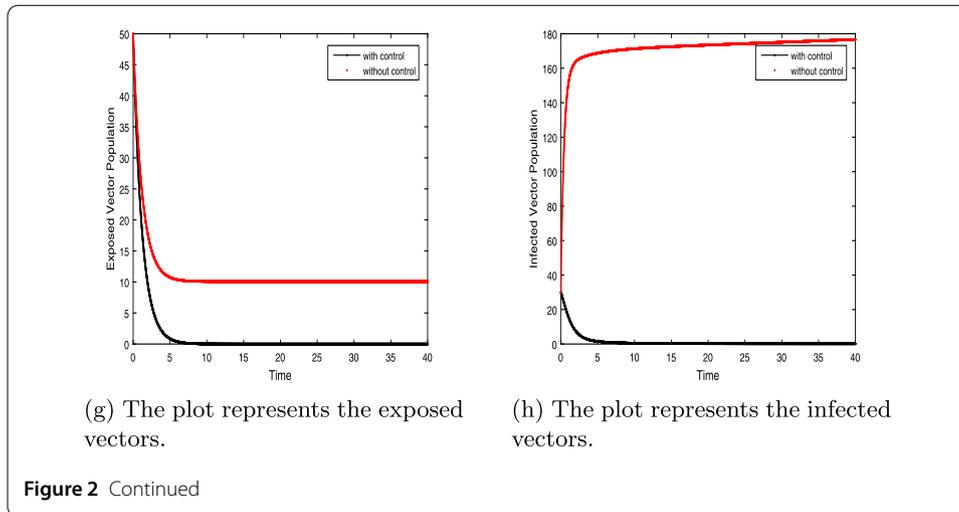


(e) The plot represents the exposed vectors.



(f) The plot represents the susceptible vectors.

Figure 2 Plots of different classes showing the difference between “with control” and “without control”



with

$$\begin{aligned}
 H^*(t) = & g_1 E_h^*(t) + g_2 I_{1h}^*(t) + g_3 I_{2h}^*(t) + g_4 N_v^*(t) + \frac{1}{2} [d_1 u_{12}^*(t) + d_2 u_{22}^*(t) + d_3 u_{32}^*(t)] \\
 & + \left[\lambda_1(t) \left(\Gamma_h - \frac{2(1 - u_1(t)) ab I_v^*(t) S_h^*(t)}{S_h^*(t) + I_v^*(t)} - \mu_h S_h^*(t) \right) \right] \\
 & + \left[\lambda_2(t) \left(\frac{2(1 - u_1^*(t)) ab I_v^*(t) S_h^*(t)}{S_h^*(t) + I_v^*(t)} - (k_1 + \theta + \mu_h) E_h^*(t) \right) \right] \\
 & + [\lambda_3(t) (k_1 E_h^*(t) - (u_2^*(t) + \beta + \mu_h + k_2) I_{1h}^*(t))] \\
 & + [\lambda_4(t) (k_2 I_{1h}^*(t) - (u_2^*(t) + \mu_h + \theta_1) I_{2h}^*(t))] \\
 & + [\lambda_5(t) (\theta E_h^*(t) + (\beta + u_2^*(t)) I_{1h}^*(t) + (\theta_1 + u_2^*(t)) I_{2h}^*(t) - \mu_h R_h^*(t))] \tag{45} \\
 & + [\lambda_6(t) (\Gamma_v - (1 - u_1^*(t)) ac I_{1h}^*(t) S_v^*(t) - (1 - u_1^*(t)) ad I_{2h}^*(t) S_v^*(t) \\
 & - (u_3(t) + \mu_v) S_v^*(t))] \\
 & + [\lambda_7(t) ((1 - u_1^*(t)) ac I_{1h}^*(t) S_v^*(t) + (1 - u_1^*(t)) ad I_{2h}^*(t) S_v^*(t) \\
 & - (u_3^*(t) + \mu_v + k_3) E_v^*(t))] \\
 & + [\lambda_8(t) (k_3 E_v^*(t) - (u_3^*(t) + \mu_v) I_v^*(t))]. \quad \square
 \end{aligned}$$

The profile of each of the state variables with and without control have been depicted in Fig. 2.

7 Conclusions

We study a five-grade Anthroponotic Cutaneous Leishmania epidemic model with harmonic mean type incidence rate. For endemic stability analysis, we consider a generalization of the Lyapunov method, called the geometrical approach, in which a second additive compound matrix is taken into account. The feasibility of our result is verified by numerical simulations. Extending our work, we can use a harmonic mean type incidence rate to reformulate a visceral model for the leishmaniasis epidemic. We can also check its stability analysis, parameter sensitivity, bifurcation analysis, and optimal control. It is strongly

recommended that proper record keeping and documentation systems for leishmaniasis be initiated by health authorities at the local, provincial, and national levels and be well maintained to identify leishmaniasis outbreaks so that control measures can be started well in time. Further, IDP camps must be monitored regularly to minimize the risk that nonendemic areas will be exposed to the disease by infected IDPs.

Acknowledgements

The authors acknowledge with thanks the support of the Deanship of Scientific Research (DSR) at King Abdulaziz University, Jeddah.

Funding

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors contributed equally to the manuscript and typed, read, and approved the final manuscript.

Author details

¹Department of Physics, University of Malakand, Chakdara Dir, Khyber Pakhtunkhwa, Pakistan. ²Department of Basic Sciences, University of Engineering and Technology, Peshawar, Khyber Pakhtunkhwa, Pakistan. ³Department of Mathematics and Statistics, University of Swat, Swat, Khyber Pakhtunkhwa, Pakistan. ⁴Department of Computer Engineering, Biruni University, Istanbul, Turkey. ⁵Department of Mathematics, Federal University Dutse, Jigawa, Nigeria. ⁶Department of Mathematics, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia.

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Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 16 December 2020 Accepted: 18 January 2021 Published online: 28 January 2021

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