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A co-infection model of dengue and leptospirosis diseases

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Abstract

In this paper an SIR deterministic mathematical model for co-infection of dengue and leptospirosis is proposed. We use a compartment model by using ordinary differential equations. The positivity of future solution of the model, the invariant region, and the stability of disease-free equilibrium point as well as endemic equilibrium point are studied. To study the stability of the equilibria, a basic reproduction number is obtained by using the next generation matrix. The robustness of the model is also investigated. To identify the effect of each parameter on the expansion or control of the diseases, sensitivity analysis is performed. The effects of treating dengue infected only, leptospirosis infected only, and co-infected individuals have been identified by using the numerical simulation. Therefore, increasing the rate of recovery and decreasing the contact rate of dengue, leptospirosis, and their co-infection have a great influence in fighting dengue, leptospirosis, and their co-infection in the community.

Keywords: Confection; Dengue fever; Leptospirosis; Stability analysis; Numerical simulation

1 Introduction

Dengue is the world's fastest spreading mosquito transmitted infectious disease. An estimated 50 million dengue infections occur annually, and nearly 2.5 billion people live in regions with potential risk of dengue transmission [1–3]. Roughly half of the world's population probably lives in regions ecologically suitable for dengue transmission [3]. Dengue is transmitted to humans by mosquitoes of *Aedes* species, which thrive around the globe in tropical and subtropical urban centers [1, 2]. The virus is transmitted by the infected female mosquito called *Aedes aegypti* [3]. There are four serotypes, DENV1–DENV4 [2, 3]. On the other hand, a zoonotic bacterial disease leptospirosis is one of the most significant neglected tropical bacterial diseases and one of the leading zoonotic causes of morbidity in the world [1, 4]. The most important reservoirs are small mammals, with large herbivores as additional important sources of infection. Pathogenic species of *Leptospira* were isolated from hundreds of mammalian species including bats and pinnipeds [5]. Leptospirosis is a global occurrence particularly in tropical and subtropical countries [5, 6]. It mainly affects vulnerable populations, with an estimated global annual incidence of 1.03 million people and 58.900 deaths [4, 6]. It is transmitted by contact with infected animal prod-

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ucts and with water, wet surfaces contaminated with animal urine [6]. Leptospirosis and dengue co-infections (LDCI) have been reported in many countries [7–10]. Co-infections occur due to simultaneous transmission of both these infections during the rainy season, and both of these infections are characterized by fever with myalgia.

Mathematical modeling has a great role in describing the dynamics of infectious diseases in a community. Several scholars have developed different models for dengue, leptospirosis, and their co-infection with other diseases to study their dynamics. For example, many mathematical models have been developed to understand dengue [11–16] and leptospirosis [17–20]. Also some co-infection models for dengue and chikungunya [21, 22] and for dengue–Zika [23, 24] have been proposed and analyzed. However, to the best of our knowledge, no one has investigated co-infection of dengue and leptospirosis. Therefore, in this paper we are interested in filling this gap.

The paper is organized as follows: Sect. 2 is devoted to the description and formulation of the model. In Sect. 3, the analysis of dengue only model, leptospirosis only model, and the co-infection model is performed. In Sect. 4 numerical simulations to give a better interpretation of the analytical results are reported. Our discussion and conclusion are presented in Sect. 5.

2 Model description and formulation

In this paper, we consider a deterministic mathematical model for co-infection of dengue and leptospirosis in a human population. The total population is divided into seven sub-classes, which are susceptible population (S), dengue infectious (I_d), leptospirosis infectious (I_l), dengue and leptospirosis co-infectious (I_{dl}), dengue recovered (R_d), leptospirosis recovered (R_l), and dengue leptospirosis co-infectious recovered (R_{dl}). Each vector population of both diseases is also divided into two susceptible vectors of dengue (S_{vd}), infected vector of dengue (I_{vd}), susceptible vector of leptospirosis (S_{vl}), and infected vector of leptospirosis (I_{vl}).

Susceptible are recruited with the rate of Π through birth or immigration, and their number increases from individuals that come from sub-classes of dengue recovered, leptospirosis recovered, and co-infectious recovered by losing their temporary immunity at a rate of σ_1 , σ_2 , and σ_3 , respectively.

The entire susceptible population join I_d compartment, when individuals can get dengue with contact rate of β_1 from a dengue only infected vectors. In a similar way, individuals can get leptospirosis by the contact rate of α_1 from a leptospirosis only infected or co-infected person with force of infection of leptospirosis $\alpha_1(I_l + I_{dl})$ or by the contact rate α_2 from the infected vector of leptospirosis (I_{vl}) and join I_l compartment.

Dengue only infected individuals also get an additional leptospirosis infection by the contact rate α_1 from a leptospirosis only infected and co-infected person with force of infection of leptospirosis $\alpha_1(I_l + I_{dl})$ or by the contact rate α_2 from the infected vector of leptospirosis (I_{vl}) and join co-infected compartment (I_{dl}). On the other hand, leptospirosis only infected individuals get an additional dengue infection by the contact rate β_1 from the infected vector of dengue (I_{vd}) and join co-infected compartment (I_{dl}).

Dengue only infected individuals recover with the rate of γ_1 and join dengue only recovered compartment (R_d). In a similar way, leptospirosis only infected individuals also recover with the rate of γ_2 and join leptospirosis only recovered compartment (R_l). The co-infected compartment also recovers with ε rate, but those individuals either recover

Table 1 Description of parameters of co-infection model (1)

Parameter	Description
Π	Human recruitment rate
Ω	Dengue vector recruitment rate
Λ	Leptospirosis vector recruitment rate
β_1	Rate of transmissibility of leptospirosis b/n dengue infected human and leptospirosis vector contact
α_1	Transmission rate from leptospirosis only infected to the susceptible human population
α_2	Transmission rate from leptospirosis vector to susceptible human population
δ_1	Disease induced death rate of human due to leptospirosis only
δ_2	Disease induced death rate of animal due to leptospirosis only
σ_1	Dengue disease waning immunity
σ_2	Leptospirosis disease waning immunity
σ_3	Dengue–leptospirosis disease waning immunity
μ	Natural death rate of human population
μ_{vd}	Natural death rate of dengue vector
μ_{vl}	Natural death rate of leptospirosis vector
ρ_1	Transmission rate from dengue only infected human to susceptible dengue vector population
ρ_2	Transmission rate from leptospirosis only infected human to susceptible leptospirosis vector population
γ_1	Rate of recovery from dengue disease
γ_2	Rate of recovery from dengue disease
ε	Rate of recovery from dengue–leptospirosis co-infection diseases
ϱ	Mortality rate related to leptospirosis vector due to the disease

only from dengue disease and join dengue only recovered compartment with probability of $\varepsilon\eta$, or recover only from leptospirosis only disease and join leptospirosis only recovered compartment with probability of $\varepsilon k(1 - \eta)$, or recover from both diseases and join co-infected recover compartment with probability of $g = \varepsilon(1 - k)(1 - \eta)$. In all compartments μ is a natural death rate of human population. Moreover, δ_1 is a dengue only caused death rate, and δ_2 is a leptospirosis caused death rate. Ω and Λ are the recruitment rates for vector population of dengue and leptospirosis, respectively. The leptospirosis and dengue vector populations have the natural death rate μ_{vl} and μ_{vd} , respectively. The description of parameters of the model are found in Table 1.

With regards to the above considerations, we have the compartmental flow diagram shown in Fig. 1. From the flow chart, the model will be governed by the following system of differential equations:

$$\begin{cases}
 \frac{dS}{dt} = \Pi + \sigma_1 R_d + \sigma_2 R_L + \sigma_3 R_{dl} - (c\beta_1 I_{vd} + \alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu)S, \\
 \frac{dI_d}{dt} = c\beta_1 I_{vd} S - (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu + \delta_1 + \gamma_1)I_d, \\
 \frac{dI_l}{dt} = (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl})S - (c\beta_1 I_{vd} + \mu + \delta_2 + \gamma_2)I_l, \\
 \frac{dI_{dl}}{dt} = (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl})I_d + c\beta_1 I_{vd} I_l - (\varepsilon + \mu + \delta_1 + \delta_2)I_{dl}, \\
 \frac{dR_d}{dt} = \gamma_1 I_d + \varepsilon\eta I_{dl} - (\mu + \sigma_1)R_d, \\
 \frac{dR_l}{dt} = \gamma_2 I_l + \varepsilon k(1 - \eta)I_{dl} - (\mu + \sigma_2)R_l, \\
 \frac{dR_{dl}}{dt} = g I_{dl} - (\mu + \sigma_3)R_{dl}, \\
 \frac{dS_{vd}}{dt} = \Omega - c\rho_1 I_d S_{vd} - \mu_{vd} S_{vd}, \\
 \frac{dI_{vd}}{dt} = c\rho_1 I_d S_{vd} - \mu_{vd} I_{vd}, \\
 \frac{dS_{vl}}{dt} = \Lambda - \rho_2 I_l S_{vl} - \mu_{vl} S_{vl}, \\
 \frac{dI_{vl}}{dt} = \rho_2 I_l S_{vl} - \mu_{vl} I_{vl}
 \end{cases} \tag{1}$$

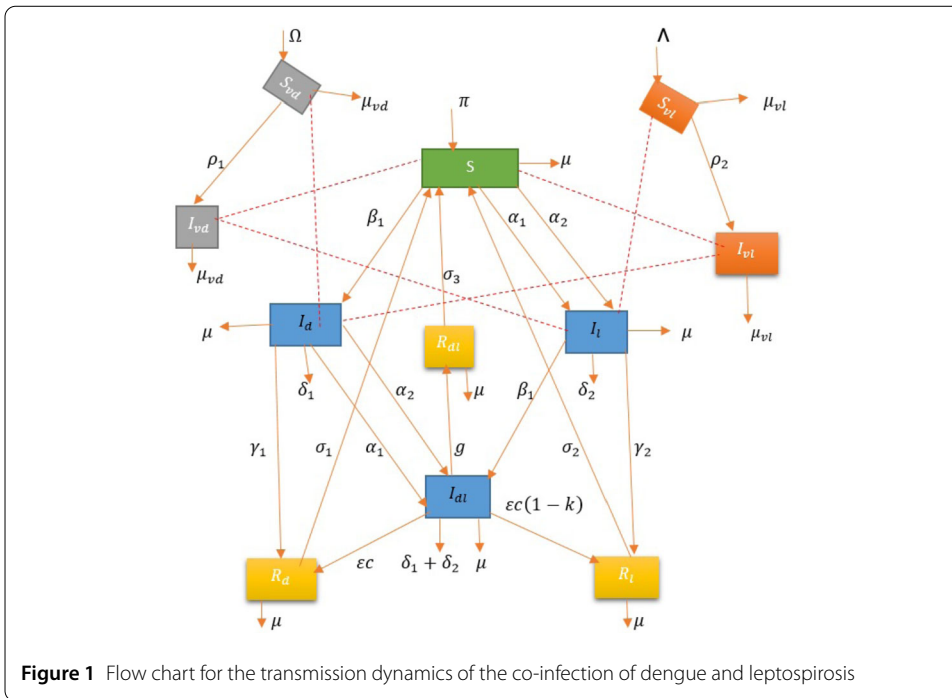


Figure 1 Flow chart for the transmission dynamics of the co-infection of dengue and leptospirosis

with the initial condition $S(0) = S_0 \geq 0, I_d(0) = I_{d,0} \geq 0, I_l(0) = I_{l,0} \geq 0, I_{dl}(0) = I_{dl,0} \geq 0, R_d(0) = R_{d,0} \geq 0, R_l(0) = R_{l,0} \geq 0, R_{dl}(0) = R_{dl,0} \geq 0, S_{vd}(0) = S_{vd,0} \geq 0, I_{vd}(0) = I_{vd,0} \geq 0, S_{vl}(0) = S_{vl,0} \geq 0, I_{vl}(0) = I_{vl,0} \geq 0$.

3 Qualitative analysis

In this section, for simplification of the work, we split the full model into sub-models, which are dengue and leptospirosis only models. The qualitative behavior of the sub-model is studied first and the full model follows.

3.1 Dengue fever only model

To get this model from equation (1), we set $I_l = I_{dl} = R_l = R_{dl} = 0, \sigma_2 = \sigma_3 = 0, I_l + I_{dl} = 0$, and then we get

$$\begin{cases} \frac{dS}{dt} = \Pi + \sigma_1 R_d - c\beta_1 I_{vd} S - \mu S, \\ \frac{dI_d}{dt} = c\beta_1 I_{vd} S - (\mu + \delta_1 + \gamma_1) I_d, \\ \frac{dR_d}{dt} = \gamma_1 I_d - (\mu + \sigma_1) R_d, \\ \frac{dS_{vd}}{dt} = \Omega - c\rho_1 I_d S_{vd} - \mu_{vd} S_{vd}, \\ \frac{dI_{vd}}{dt} = c\rho_1 I_d S_{vd} - \mu_{vd} I_{vd}. \end{cases} \tag{2}$$

3.1.1 Invariant region

To get an invariant region, which shows as the solution is bounded, the total human population of the model is $N_h = S + I_d + R_d$. Differentiating N_h both sides and substituting respective expressions of $\frac{dS}{dt}, \frac{dI_d}{dt}$, and $\frac{dR_d}{dt}$ from equation (2), we get

$$\frac{dN_h}{dt} = \Pi - \mu N_h - \delta_1 I_d. \tag{3}$$

If we are not considering death from dengue fever, then equation (3) becomes

$$\frac{dN_h}{dt} \leq \Pi - \mu N. \tag{4}$$

Solving equation (4), we get

$$\mathcal{D}_h = \left\{ (S, I_d, R_d) \in \mathcal{R}_+^3 : 0 \leq N_h \leq \frac{\Pi}{\mu} \right\}. \tag{5}$$

Similarly, for the vector population $N_{vd} = S_{vl} + I_{vl}$, we have

$$\mathcal{D}_{vd} = \left\{ (S_{vd}, I_{vd}) \in \mathcal{R}_+^2 : 0 \leq N_{vd} \leq \frac{\Omega}{\mu_{vd}} \right\}.$$

Therefore, all the solution set of (2) is bounded in $\mathcal{D} = \mathcal{D}_{hd} \times \mathcal{D}_{vd}$.

3.1.2 Positivity of solutions

Theorem 3.1 *If the initial value $S_0 \geq 0, I_{d0} \geq 0, I_{dl0} \geq 0, R_{d0} \geq 0, S_{vd0} \geq 0, I_{vd0} \geq 0$, then the solutions of the dengue only infected model are nonnegative.*

Proof From the first equation of the system in equation (2)

$$\frac{dS}{dt} = \Pi + \sigma_1 R_d - c\beta_1 I_{vd} S - \mu S,$$

which can be taken as

$$\frac{dS}{dt} \geq -\mu S, \tag{6}$$

after evaluating equation (6), we obtain

$$S \geq S(0)e^{-\mu t}.$$

Similarly, we obtain

$$\begin{aligned} I_d &\geq I_d(0)e^{-(\mu+\delta_1+\gamma_1)t}, & R_d &\geq R_d(0)e^{-(\mu+\sigma_1)t}, \\ S_{vd} &\geq S_{vd}(0)e^{-\mu_{vd}t}, & I_{vd} &\geq I_{vd}(0)e^{-\mu_{vd}t}. \end{aligned}$$

Therefore, all the solution sets are nonnegative for $t \geq 0$. □

3.1.3 Disease-free equilibrium (DFEP)

By equating equation (2) to zero and substituting $I_d = R_d = I_{vd} = 0$, we obtain DFEP $E_{0d} = (\frac{\Pi}{\mu}, 0, 0, \frac{\Omega}{\mu_{vd}}, 0)$.

3.1.4 Basic reproduction number

The basic reproduction number is an average number of secondary cases of infection when a single infectious individual is introduced into the total susceptible population. To obtain

(\mathcal{R}_{0d}), the next generation matrix method that was formulated by [25] is used, and it is given by

$$\mathcal{R}_{0d} = \sqrt{\frac{c^2 \rho_1 \beta_1 \Pi \Omega}{\mu \mu_{vd}^2 (\mu + \delta_1 + \gamma_1)}}. \tag{7}$$

3.1.5 Local stability of DFEP

Theorem 3.2 *DFEP is locally asymptotically stable if $\mathcal{R}_{0d} < 1$ and unstable if $\mathcal{R}_{0d} > 1$.*

Proof The Jacobian matrix of the dengue only model at DFEP is given by

$$J = \begin{pmatrix} -\mu & 0 & \sigma_1 & 0 & -\frac{c\beta_1\Pi}{\mu} \\ 0 & -\delta_1 - \gamma_1 - \mu & 0 & 0 & \frac{c\beta_1\Pi}{\mu} \\ 0 & \gamma_1 & -\sigma_1 - \mu & 0 & 0 \\ 0 & -\frac{c\rho_1\Omega}{\mu_{vd}} & 0 & -\mu_{vd} & 0 \\ 0 & \frac{c\rho_1\Omega}{\mu_{vd}} & 0 & 0 & -\mu_{vd} \end{pmatrix}. \tag{8}$$

The eigenvalues of the matrix in (8), $-\mu$, $-(\sigma_1 + \mu)$ and $-\mu_{vd}$ are clearly negative. The other two eigenvalues can be obtained from the quadratic equation given by

$$p(\lambda) = \lambda^2 + \psi_1 \lambda + \psi_2, \tag{9}$$

where

$$\begin{aligned} \psi_1 &= \delta_1 + \gamma_1 + \mu + \mu_{vd} > 0, \\ \psi_2 &= \frac{-c^2 \rho_1 \Omega \beta_1 \Pi + \mu^2 \mu_{vd}^2 + \delta_1 \mu_{vd}^2 \mu + \gamma_1 \mu_{vd}^2 \mu}{\mu \mu_{vd}} \\ &= \mu_{vd} (\delta_1 + \gamma_1 + \mu) (1 - \mathcal{R}_{0d}^2). \end{aligned}$$

Here, it follows from Routh–Hurwitz criteria $\psi_1 > 0$ and $\psi_2 > 0$. Thus, all the eigenvalues of the matrix in equation (9) have negative real parts if $\mathcal{R}_{0d} < 1$. Hence DFEP is locally asymptotically stable. □

3.1.6 Existence of endemic equilibrium point (EEP)

The endemic equilibrium point is denoted by $E^* = (S^*, I_d^*, R_d^*, S_{vd}^*, I_{vd}^*)$ and it occurs when the disease persists in the community.

Lemma 3.3 *For $\mathcal{R}_{0d} > 1$ a unique EEP E^* exists and no EEP otherwise.*

Proof To obtain it, we equate all the model equations in equation (2) to zero. Then we obtain

$$\begin{cases} S^* = \frac{\mu_{vd}(\delta_1 + \gamma_1 + \mu)\varphi_1}{\rho_1\varphi_2}, \\ I_d^* = \frac{(\sigma_1 + \mu)(\mathcal{R}_{0d}^2 - 1)}{\mu\mu_{vd}^2(\delta_1 + \gamma_1 + \mu)\rho_1\varphi_2}, \\ R_d^* = \frac{\gamma_1(\mathcal{R}_{0d}^2 - 1)}{\mu\mu_{vd}^2(\delta_1 + \gamma_1 + \mu)\rho_1\varphi_2}, \\ S_{vd}^* = \frac{\varphi_2}{\beta\varphi_1}, \\ I_{vd}^* = \frac{(\sigma_1 + \mu)(\mathcal{R}_{0d}^2 - 1)}{\mu\mu_{vd}^2(\delta_1 + \gamma_1 + \mu)\varphi_1}, \end{cases} \tag{10}$$

where

$$\begin{aligned} \varphi_1 &= \Pi\rho_1(\mu + \sigma_1) + \mu\mu_{vd}(\mu + \delta_1 + \gamma_1 + \sigma_1) + \delta_1\sigma_1\mu_{vd}, \\ \varphi_2 &= \Omega\beta_1\delta_1\sigma_1 + \Omega\mu\beta_1(\mu + \delta_1 + \gamma_1 + \sigma_1) + \mu^2\mu_{vd}(\mu + \delta_1 + \gamma_1 + \sigma_1) + \mu\mu_{vd}\sigma_1(\delta_1 + \gamma_1). \square \end{aligned}$$

3.1.7 Existence of backward bifurcation of dengue only model

We investigated the nature of the bifurcation by using the method introduced in [26], which is based on center manifold theory [26]. In order to apply theory, the following rearrangement and modification of variables are done on the submodel in equation (2). We let $S = z_1, I_d = z_2, R_d = z_3, S_{vd} = z_4,$ and $I_{vd} = z_5$. In addition, using vector notation $z = (z_1, z_2, z_3, z_4, z_5)^T$, formulated as $\frac{dz}{dt} = F(z)$, with $F = (f_1, f_2, f_3, f_4, f_5)^T$ given in the following, we chose β_1 as a bifurcation parameter and solve $\mathcal{R}_{0d} = 1$, which leads to

$$\begin{aligned} \frac{dz_1}{dt} &= f_1 = \Pi + \sigma_1 z_3 - c\beta_1 z_5 z_1 - \mu z_1, \\ \frac{dz_2}{dt} &= f_2 = c\beta_1 z_5 z_1 - (\mu + \delta_1 + \gamma_1) z_2, \\ \frac{dz_3}{dt} &= f_3 = \gamma_1 z_2 - (\mu + \sigma_1) z_3, \\ \frac{dz_4}{dt} &= f_4 = \Omega - c\rho_1 z_2 z_4 - \mu_{vd} z_4, \\ \frac{dz_5}{dt} &= f_5 = c\rho_1 z_2 z_4 - \mu_{vd} z_5, \end{aligned} \tag{11}$$

where

$$\beta_1 = \beta_1^* = \frac{\mu\mu_{vd}^2(\mu + \delta_1 + \gamma_1)}{c^2\rho_1\Pi\Omega}.$$

The Jacobian matrix evaluated at DFEP is given by $(z_1 = \frac{\Pi}{\mu}, z_2 = 0; z_3 = 0, z_4 = \frac{\Omega}{\mu_{vd}}, z_5 = 0)$:

$$J = \begin{pmatrix} -\mu & 0 & \sigma_1 & 0 & -\frac{c\beta_1^*\Pi}{\mu} \\ 0 & -(\mu + \delta_1 + \gamma_1) & 0 & 0 & \frac{c\beta_1^*\Pi}{\mu} \\ 0 & \gamma_1 & -(\mu + \sigma_1) & 0 & 0 \\ 0 & -\frac{c\rho_1\Omega}{\mu_{vd}} & 0 & -\mu_{vd} & 0 \\ 0 & \frac{c\rho_1\Omega}{\mu_{vd}} & 0 & 0 & -\mu_{vd} \end{pmatrix}. \tag{12}$$

The right eigenvector $u = (u_1, u_2, u_3, u_4, u_5)^T$ associated with the simple zero eigenvalue can be obtained as follows:

$$\begin{aligned}
 u_1 &= \frac{\sigma_1 \gamma_1 - (\mu + \sigma_1)(\mu + \delta_1 + \gamma_1)}{\mu(\mu + \sigma_1)} u_2, \\
 u_2 &= u_2 > 0, \\
 u_3 &= \frac{\gamma_1}{\mu + \sigma_1} u_2, \\
 u_4 &= -\frac{c \rho_1 \Omega}{\mu_{vd}^2} u_2, \\
 u_5 &= \frac{c \rho_1 \Omega}{\mu_{vd}^2} u_2.
 \end{aligned}$$

Similarly, we obtain the left eigenvector $v = (v_1, v_2, v_3, v_4, v_5)$ associated with the simple zero eigenvalue and given by

$$v_1 = v_3 = v_4 = 0, \quad v_2 = v_2 > 0, \quad v_5 = \frac{\mu_{vd}(\mu + \delta_1 + \gamma_1)}{c \rho_1 \Omega} v_2.$$

Since the first, third, and fourth components of v are zero, we do not need the derivatives of $f_1, f_3,$ and f_4 . From the derivatives of f_2 and f_5 , the only ones that are nonzero are the following:

$$\frac{\partial^2 f_2}{\partial z_1 \partial z_5} = \frac{\partial^2 f_2}{\partial z_5 \partial z_1} = c \beta_1^*, \quad \frac{\partial^2 f_5}{\partial z_2 \partial z_4} = \frac{\partial^2 f_5}{\partial z_4 \partial z_2} = c \rho_1, \quad \frac{\partial^2 f_2}{\partial z_5 \partial \beta_1} = c z_1^*$$

and all the other partial derivatives are zero. The direction of the bifurcation at $\mathcal{R}_{0d} = 1$ is determined by the signs of the bifurcation coefficients a and b , obtained from the above partial derivatives, given respectively by

$$\begin{aligned}
 a &= 2v_2 u_1 u_5 \frac{\partial^2 f_2}{\partial z_1 \partial z_5} + 2v_5 u_2 u_4 \frac{\partial^2 f_5}{\partial z_4 \partial z_2} \\
 &= -2u_2 \left(\frac{\mu + \delta_1 + \gamma_1}{\mu_{vd} \Pi(\mu + \sigma_1)} \right) [(\mu + \sigma_1)(\mu + \delta_1 + \gamma_1) + \rho_1 \Pi(\mu + \sigma_1) - \sigma_1 \gamma_1 \mu_{vd}]
 \end{aligned}$$

and

$$b = v_2 u_5 \frac{\partial^2 f_2}{\partial z_5 \partial \beta_1^*} = v_2 u_5 c z_1^* = \frac{c \Pi \rho_1 \beta \Omega}{\mu \mu_{vd}^2} > 0. \tag{13}$$

By the fact that coefficient b is positive, it shows that the sign of coefficient a determines the local dynamics around DFEP for β_1 . It is clearly seen that system (11) undergoes backward bifurcation, and therefore we propose the following theorem.

Theorem 3.4 *The model in system (1) exhibits backward bifurcation at $\mathcal{R}_{0d} = 1$ and the disease-free equilibrium may not be globally stable.*

3.2 Leptospirosis only model

To get this model from equation (1), we set $I_d = I_{dl} = R_d = R_{dl} = 0, \sigma_1 = \sigma_3 = 0$, and then we get

$$\begin{cases} \frac{dS}{dt} = \Pi + \sigma_2 R_l - (\alpha_1 I_l + \alpha_2 I_{vl} + \mu)S, \\ \frac{dI_l}{dt} = (\alpha_1 I_l + \alpha_2 I_{vl})S - (\mu + \delta_2 + \gamma_2)I_l, \\ \frac{dR_l}{dt} = \gamma_2 I_l - (\mu + \sigma_2)R_l, \\ \frac{dS_{vl}}{dt} = \Lambda - \rho_2 I_l S_{vl} - \mu_{vl} S_{vl}, \\ \frac{dI_{vl}}{dt} = \rho_2 I_l S_{vl} - \mu_{vl} I_{vl} \end{cases} \tag{14}$$

3.2.1 Invariant region

To get an invariant region, the total population of the model is $N_{hl} = S + I_l + R_l$. Then the derivative of N_{hl} with respect to time gives

$$\frac{dN_{hl}}{dt} = \Pi - \mu N_{hl} - \delta_2 I_l. \tag{15}$$

If we are not considering death from leptospirosis, then equation (15) becomes

$$\frac{dN_{hl}}{dt} \leq \Pi - \mu N_{hl}. \tag{16}$$

After solving equation (16), we get

$$\mathcal{D}_l = \left\{ (S, I_l, R_l) \in \mathfrak{R}_+^3 : 0 \leq N_{hl} \leq \frac{\Pi}{\mu} \right\}. \tag{17}$$

Similarly, for the vector population $N_{vl} = S_{vl} + I_{vl}$, we have

$$\mathcal{D}_{vl} = \left\{ (S_{vl}, I_{vl}) \in \mathfrak{R}_+^2 : 0 \leq N_{vl} \leq \frac{\Lambda}{\mu_{vl}} \right\}.$$

Therefore, all the solution set of the model in equation (14) is bounded in $\mathcal{D}_2 = \mathcal{D}_l \times \mathcal{D}_{vl}$.

3.2.2 Positivity of solutions

Theorem 3.5 *If the initial value $S_0 \geq 0, I_{l0} \geq 0, R_{l0} \geq 0, S_{vl0} \geq 0, I_{vl0} \geq 0$ and the solutions of the leptospirosis only infected model are nonnegative.*

Proof To show solutions of the model are positive, first we take $\frac{dS}{dt}$ from equation (14):

$$\frac{dS}{dt} = \Pi + \sigma_2 R_l - (\alpha_1 I_l + \alpha_2 I_{vl} + \mu)S,$$

which can be rewritten as

$$\frac{dS}{dt} \geq -\mu S. \tag{18}$$

Solving equation (18), we get

$$S \geq S(0)e^{-\mu t}.$$

Similarly, we obtain

$$\begin{aligned}
 I_l &\geq I_l(0)e^{-(\mu+\delta_2+\gamma_2)t}, & R_l &\geq R_l(0)e^{-(\mu+\sigma_2)t}, \\
 S_{vl} &\geq S_{vl}(0)e^{-\mu_{vl}t}, & I_{vl} &\geq I_{vl}(0)e^{-\mu_{vl}t}.
 \end{aligned}$$

Therefore, all the solution sets are positive for $t \geq 0$. □

3.2.3 Disease-free equilibrium (DFEP)

Equating equation (14) to zero and substituting $I_l = 0, R_l = 0, I_{vl} = 0$, we obtain the DFEP $E_{0l} = (\frac{\Pi}{\mu}, 0, 0, \frac{\Lambda}{\mu_{vl}}, 0)$.

3.2.4 Basic reproduction number

The basic reproduction number (\mathcal{R}_{0l}) is obtained using the next generation matrix method that was formulated by [25], and it is given by

$$\mathcal{R}_{0l} = \frac{\alpha_1 \Pi \mu_{vl}^2 + \alpha_2 \rho_2 \Pi \Lambda}{\mu \mu_{vl}^2 (\mu + \delta_2 + \gamma_2)} = \mathcal{R}_{0hl} + \mathcal{R}_{0vl}, \tag{19}$$

where $\mathcal{R}_{0hl} = \frac{\alpha_1 \Pi}{\mu(\mu+\delta_2+\gamma_2)}$ and $\mathcal{R}_{0vl} = \frac{\alpha_2 \rho_2 \Pi \Lambda}{\mu \mu_{vl}^2 (\mu+\delta_2+\gamma_2)}$.

3.2.5 Local stability of DFEP

Theorem 3.6 *DFEP is locally asymptotically stable if $\mathcal{R}_{0l} < 1$ and unstable if $\mathcal{R}_{0l} > 1$.*

Proof The Jacobian matrix at DFEP is given by

$$J = \begin{pmatrix} -\mu & -\frac{\alpha_1 \Pi}{\mu} & \sigma_2 & 0 & -\frac{\alpha_2 \Pi}{\mu} \\ 0 & \frac{\alpha_1 \Pi}{\mu} - (\mu + \delta_2 + \gamma_2) & 0 & 0 & \frac{\alpha_2 \Pi}{\mu} \\ 0 & \gamma_2 & -(\sigma_2 + \mu) & 0 & 0 \\ 0 & -\frac{\rho_2 \Lambda}{\mu_{vl}} & 0 & -\mu_{vl} & 0 \\ 0 & \frac{\rho_2 \Lambda}{\mu_{vl}} & 0 & 0 & -\mu_{vl} \end{pmatrix}. \tag{20}$$

The eigenvalues $-\mu, -(\sigma_2 + \mu)$ and $-\mu_{vl}$ are clearly negative. The other two eigenvalues can be obtained from the quadratic equation given by

$$p(\lambda) = \lambda^2 + \psi_1 \lambda + \psi_2,$$

where

$$\begin{aligned}
 \psi_1 &= \frac{-\alpha_1 \Pi + \mu^2 + \delta_2 \mu + \gamma_2 \mu + \mu_{vl} \mu}{\mu}, \\
 \psi_2 &= \frac{\rho_2 \Lambda \alpha_2 \Pi + \Pi \alpha_1 \mu_{vl}^2 - \mu^2 \mu_{vl}^2 - \mu \delta_2 \mu_{vl}^2 - \mu \gamma_2 \mu_{vl}^2}{\mu_{vl}}.
 \end{aligned}$$

We applied Routh–Hurwitz criteria, and by the principle, the quadratic equation has a strictly negative real root iff $\psi_1 > 0, \psi_2 > 0$, and $\psi_1 \psi_2 > 0$.

$$\psi_1 = \frac{-\alpha_1 \Pi + \mu^2 + \delta_2 \mu + \gamma_2 \mu + \mu_{vl} \mu}{\mu} = (\mu + \delta_2 + \gamma_2) \left[1 + \frac{\mu_{vl}}{\mu(\mu + \delta_2 + \gamma_2)} - \mathcal{R}_{0hl} \right] > 0,$$

$$\psi_2 = \frac{\rho_2 \Lambda \alpha_2 \Pi + \Pi \alpha_1 \mu_{vl}^2 - \mu^2 \mu_{vl}^2 - \mu \delta_2 \mu_{vl}^2 - \mu \gamma_2 \mu_{vl}^2}{\mu_{vl}} = \mu_{vl}(\mu + \delta_2 + \gamma_2)(1 - \mathcal{R}_{0l}) > 0.$$

Hence DFEP is locally asymptotically stable if $\mathfrak{R}_{0l} < 1$. □

3.2.6 Global stability of DFEP

Theorem 3.7 *The equilibrium point $E_0 = (X^*, 0)$ of system (14) is globally asymptotically stable if $\mathcal{R}_{l0} < 1$ and conditions (i) and (ii) from the theorem in [26] are satisfied.*

Proof To investigate the global stability of DFEP, we use the technique implemented by Castillo-Chavez and Song [26]. From equation (14), we can get $F(X, Z)$ and $G(X, Z)$, where $X = (S, R_l, S_{vl}) \in \mathcal{R}^3$ denotes uninfected populations and $Z = (I_l, I_{vl}) \in \mathcal{R}^2$ denotes infected populations:

$$F(X, Z) = \begin{pmatrix} \Pi + \sigma_2 R_l - (\alpha_1 I_l + \alpha_2 I_{vl} + \mu) S \\ \gamma_2 I_l - (\mu + \sigma_2) R_l \\ \Lambda - \rho_2 I_l S_{vl} - \mu_{vl} S_{vl} \end{pmatrix}$$

and

$$G(X, Z) = \begin{pmatrix} (\alpha_1 I_l + \alpha_2 I_{vl}) S - (\mu + \delta_2 + \gamma_2) I_l \\ \rho_2 I_l S_{vl} - \mu_{vl} I_{vl} \end{pmatrix}.$$

Now consider the reduced system $\frac{dX}{dt} = F(X, 0)$:

$$\frac{dX}{dt} = \begin{cases} \frac{dS}{dt} = \Pi - \mu S, \\ \frac{dS_{vl}}{dt} = \Lambda - \mu_{vl} S_{vl}. \end{cases} \tag{21}$$

$X^* = (\frac{\Pi}{\mu}, 0, \frac{\Lambda}{\mu_{vl}})$ is a globally asymptotically stable equilibrium point for the reduced system $\frac{dX}{dt} = F(X, 0)$. This can be verified. From the solution of the first equation in equation (21) we obtain $S(t) = \frac{\Pi}{\mu} + (S(0) - \frac{\Pi}{\mu})e^{-\mu t}$, which approaches $\frac{\Pi}{\mu}$ as $t \rightarrow \infty$; and from the second equation of equation (21) we get $S_{vl} = \frac{\Lambda}{\mu_{vl}} + (S_{vl}(0) - \frac{\Lambda}{\mu_{vl}})e^{-\mu_{vl} t}$, which approaches $\frac{\Lambda}{\mu_{vl}}$ and $\frac{\Lambda}{\mu_{vl}}$ as $t \rightarrow \infty$. We note that this asymptomatic dynamics is independent of the initial conditions in Ω , therefore the convergence of the solutions of the reduced system (21) is global in Ω . Now we compute

$$D_Z G(X^*, 0) = \begin{pmatrix} \frac{\alpha_1 \Pi}{\mu} - (\delta_2 + \gamma_2 + \mu) & \frac{\alpha_2 \Pi}{\mu} \\ \frac{\rho_2 \Lambda}{\mu_{vl}} & -\mu_{vl} \end{pmatrix}.$$

Then $G(X, Z)$ can be written as

$$G(X, Z) = D_Z G(X^*, 0)Z - \hat{G}(X, Z),$$

and we want to show $\hat{G}(X; Z) \geq 0$, which is obtained as follows:

$$\hat{G}(X, Z) = \begin{pmatrix} \alpha_1 (\frac{\Pi}{\mu} - S) I_l + \alpha_2 (\frac{\Pi}{\mu} - S) I_{vl} \\ \rho_2 (\frac{\Lambda}{\mu_{vl}} - S_{vl}) I_l \end{pmatrix}. \tag{22}$$

Here, $\frac{\Pi}{\mu} \geq S$ and $\frac{\Lambda}{\mu_{vl}} \geq S_{vl}$. Hence it is clear that equation $\hat{G}(X, Z) \geq 0$ for all $(X, Z) \in \Omega$. Therefore, this proves that DFEP is globally asymptotically stable when $\mathcal{R}_{0l} < 1$. Hence the endemic equilibrium point does not coexist with the disease-free equilibrium point when $\mathcal{R}_{0l} < 1$. This implies that the model exhibits forward bifurcation at $\mathcal{R}_{0l} = 1$. From this we can say that the disease can be eliminated from the population irrespective of the initial infectious population. \square

3.2.7 Endemic equilibrium (EEP)

The endemic equilibrium is denoted by $E_p^* = (S^*, I_l^*, R_l^*, S_{vl}^*, I_{vl}^*)$, and it occurs when the disease persists in the community.

Lemma 3.8 *A unique endemic equilibrium exists if one of the following holds true:*

- (i) if $C < 0 \iff \mathcal{R}_{0l} > 1$;
- (ii) if $B < 0$ and $C = 0$ or $B^2 - 4AC = 0$.

Proof To obtain it, we equate all the model equations (14) to zero. Then we obtain

$$\begin{cases} S^* = \frac{\mu_{vl}(\mu + \delta_2 + \gamma_2)(\rho_2 I_l^* + \mu_{vl})}{\alpha_2 \rho_2 \Lambda + \alpha_1 \mu_{vl}(\rho_2 I_l^* + \mu_{vl})}, \\ R_l^* = \frac{\gamma_2 I_l^*}{\mu + \sigma_2}, \\ S_{vl}^* = \frac{\Lambda}{\rho_2 I_l^* + \mu_{vl}}, \\ I_{vl}^* = \frac{\rho_2 \Lambda I_l^*}{\mu_{vl}(\rho_2 I_l^* + \mu_{vl})}. \end{cases} \tag{23}$$

When we substitute S^* in the first equation of the model in (14), we get

$$A I_l^{*2} + B I_l^* + C = 0, \tag{24}$$

where

$$\begin{aligned} A &= \alpha_1 \rho_2 [(\mu + \delta_2 + \gamma_2)(\sigma_2 + \mu) - \sigma_2 \gamma_2], \\ B &= (\sigma_2 + \mu)(\mu + \delta_2 + \gamma_2)[\alpha_1 \mu_{vl} + \alpha_2 \rho_2 \Lambda + \mu \rho_2] - [(\sigma_2 + \mu)\alpha_1 \Pi \rho_1 + \sigma_2 \gamma_2 \alpha_1 \rho_2], \\ C &= \mu \mu_{vl}(\sigma_2 + \mu)(\mu + \delta_2 + \gamma_2)[1 - \mathcal{R}_{0l}]. \end{aligned}$$

It is important to note that the coefficient A is positive with B and C having different signs. There is unique EE whenever condition (i) or (ii) holds true. Also the other condition we did not mention is that there are two endemic equilibria if $C > 0$, $B < 0$, and $B^2 - 4AC > 0$. However, this does not happen because we proved that DEFP of leptospirosis only model is globally asymptotically stable, which means that there is no way that the endemic equilibrium point co-exists with DFEP when $\mathcal{R}_{0l} < 1$. \square

3.3 Dengue–leptospirosis co-infection model

The model in equation (1) is dengue and leptospirosis co-infection equation with $S(0) = S_0$, $I_d(0) = I_{d0}$, $I_l(0) = I_{l0}$, $I_{dl}(0) = I_{dl0}$, $R_d(0) = R_{d0}$, $R_l(0) = R_{l0}$, $R_{dl}(0) = R_{dl0}$, $S_{vd}(0) = S_{vd0}$, $I_{vd}(0) = I_{vd0}$, $S_{vl}(0) = S_{vl0}$, $I_{vl}(0) = I_{vl0}$ being nonnegative initial values.

3.3.1 Invariant region

In this section, we obtain a region in which the solution of (1) is bounded. For this model the total human population is $N = S + I_d + I_l + I_{dl} + R_d + R_l + R_{dl}$. Then, after differentiating N with respect to time and substituting each equation from equation (1) to the respective place, we get

$$\frac{dN}{dt} = \Pi - \mu N - \delta_1(I_d + I_{dl}) + \delta_2(I_l + I_{dl}). \tag{25}$$

If we do not consider death from leptospirosis, dengue, and the co-infection, then equation (25) becomes

$$\frac{dN}{dt} \leq \Pi - \mu N. \tag{26}$$

After solving equation (26) and evaluating it as time tends to infinity, we get

$$\mathcal{D}_h = \left\{ (S, I_d, I_l, I_{dl}, R_d, R_l, R_{dl}) \in \mathcal{R}^7 : 0 \leq N \leq \frac{\Pi}{\mu} \right\}.$$

Similarly, for vector population of dengue, if there is no discharge of virus from the infectious, then

$$\begin{aligned} \frac{dN_{vd}}{dt} &= \Omega - \mu_{vd}N_{vd}, \tag{27} \\ \mathcal{D}_{vd} &= \left\{ (S_{vd}, I_{vd}) \in \mathcal{R}_+^2 : N_{vd}(t) \leq \frac{\Omega}{\mu_{vd}} \right\}. \end{aligned}$$

Also, for vector population of leptospirosis, if there is no discharge of bacteria from the infectious, then

$$\begin{aligned} \frac{dN_{vl}}{dt} &= \Lambda - \mu_{vl}N_{vl}, \tag{28} \\ \mathcal{D}_{vl} &= \left\{ (S_{vl}, I_{vl}) \in \mathcal{R}_+^2 : N_{vl}(t) \leq \frac{\Lambda}{\mu_{vl}} \right\}. \end{aligned}$$

Therefore, the feasible solution set for the dengue–leptospirosis co-infection model is given by

$$\mathcal{D} = \mathcal{D}_h \times \mathcal{D}_{vd} \times \mathcal{D}_{vl} = \left\{ (S, I_d, I_l, I_{dl}, R_d, R_l, R_{dl}, S_{vd}, I_{vd}, S_{vl}, I_{vl}) \in \mathcal{R}_+^{11} \right\}. \tag{29}$$

Therefore, all the solution set of equation (1) is bounded in $\mathcal{D} = \mathcal{D}_h \times \mathcal{D}_{vd} \times \mathcal{D}_{vl}$.

3.3.2 Positivity of solutions

Theorem 3.9 *If $S_0 > 0, I_{d0} > 0, I_{l0} > 0, I_{dl0} > 0, R_{d0} > 0, R_{l0} > 0, R_{dl0} > 0, S_{vd0} > 0, I_{vd0} > 0, S_{vl0} > 0, I_{vl0} > 0$, then the future time solutions of the dengue–leptospirosis co-infection population are positive.*

Proof We let $\tau = \sup\{t > 0 : S_0(t_1) > 0, I_{d0}(t_1) > 0, I_{l0}(t_1) > 0, I_{dl0}(t_1) > 0, R_{d0}(t_1) > 0, R_{l0}(t_1) > 0, R_{dl0}(t_1) > 0, S_{vd0}(t_1) > 0, I_{vd0}(t_1) > 0, S_{vl0}(t_1) > 0, I_{vl0}(t_1) > 0 \text{ for all } t_1 \in [0, t]\}$. Since $S_0 \geq 0,$

$I_{d0} \geq 0, I_{l0} \geq 0, I_{dl0} \geq 0, R_{d0} \geq 0, R_{l0} \geq 0, R_{dl0} \geq 0, S_{vd0} \geq 0, I_{vd0} \geq 0, S_{vl0} \geq 0,$ and $I_{vl0} \geq 0,$ hence $\tau > 0.$ If $\tau < \infty,$ then $S_0(t), I_{d0}(t), I_{l0}(t), I_{dl0}(t), R_{d0}(t), R_{l0}(t), R_{dl0}(t), S_{vd0}(t), I_{vd0}(t), S_{vl0}(t), I_{vl0}(t)$ are zero at $t_1.$ To show that solution of the model is positive, first we take $\frac{dS}{dt}$ from Eq. (1).

$$\frac{dS}{dt} = \Pi + \sigma_1 R_d + \sigma_2 R_L + \sigma_3 R_{dl} - (c\beta_1 I_{vd} + \alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu)S. \tag{30}$$

Using the variation of constants formula, the solution of equation (30) at τ is given by

$$S(\tau) = S(0) \exp\left[-\int_0^\tau ((c\beta_1 I_{vd} + \alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu)S(dS))\right] + \int_0^\tau (\Pi + \sigma_1 R_d + \sigma_2 R_L + \sigma_3 R_{dl}) \times \exp\left[-\int_S^\tau ((c\beta_1 I_{vd} + \alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu)(t_1) dt_1)\right].$$

Moreover, since all the variables are positive in $[0, \tau],$ then $S(\tau) > 0.$

It can be shown in a similar way that $I_d(\tau) > 0, I_l(\tau) > 0, I_{dl}(\tau) > 0, R_d(\tau) > 0, R_l(\tau) > 0, R_{dl}(\tau) > 0, S_{vd}(\tau) > 0, I_{vd}(\tau) > 0, S_{vl}(\tau) > 0,$ and $I_{vl}(\tau) > 0,$ which is a contradiction. Hence $\tau = \infty.$ □

3.3.3 Disease-free equilibrium (DFEP)

Equating equation (1) to zero and substituting $I_d = 0, I_l = 0, I_{dl} = 0, R_d = 0, R_l = 0, R_{dl} = 0, I_{vd} = 0, I_{vl} = 0,$ we obtain the DFEP $E_0 = (\frac{\Pi}{\mu}, 0, 0, 0, 0, 0, 0, \frac{\Omega}{\mu_{vd}}, 0, \frac{\Delta}{\mu_{vl}}, 0).$

3.3.4 Basic reproduction number

To obtain $(\mathcal{R}_0),$ we use the next generation matrix method [25]. Let us consider the infective compartments of the model

$$\begin{cases} \frac{dI_d}{dt} = c\beta_1 I_{vd}S - (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu + \delta_1 + \gamma_1)I_d, \\ \frac{dI_l}{dt} = (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl})S - (c\beta_1 I_{vd} + \mu + \delta_2 + \gamma_2)I_l, \\ \frac{dI_{dl}}{dt} = (\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl})I_d + c\beta_1 I_{vd}I_l - (\epsilon + \mu + \delta_1 + \delta_2)I_{dl}, \\ \frac{dI_{vd}}{dt} = c\rho_1 I_d S_{vd} - \mu_{vd} I_{vd}, \\ \frac{dI_{vl}}{dt} = \rho_2 I_l S_{vl} - \mu_{vl} I_{vl}. \end{cases} \tag{31}$$

Then, by the principle of next-generation matrix, we obtain \mathcal{F} and $\mathcal{V},$ and evaluating the Jacobians at DFEP, we get

$$\mathcal{F} = \begin{pmatrix} 0 & 0 & 0 & \frac{c\beta_1 \Pi}{\mu} & 0 \\ 0 & \frac{\alpha_1 \Pi}{\mu} & \frac{\alpha_1 \Pi}{\mu} & 0 & \frac{\alpha_2 \Pi}{\mu} \\ 0 & 0 & 0 & 0 & 0 \\ \frac{c\rho_1 \Omega}{\mu_{vd}} & 0 & 0 & 0 & 0 \\ 0 & \frac{\rho_2 \Delta}{\mu_{vl}} & 0 & 0 & 0 \end{pmatrix} \text{ and } \mathcal{V} = \begin{pmatrix} \varsigma_1 & 0 & 0 & 0 & 0 \\ 0 & \varsigma_2 & 0 & 0 & 0 \\ 0 & 0 & \varsigma_3 & 0 & 0 \\ 0 & 0 & 0 & \mu_{vd} & 0 \\ 0 & 0 & 0 & 0 & \mu_{vl} \end{pmatrix}, \tag{32}$$

where

$$\varsigma_1 = \delta_1 + \gamma_1 + \mu, \quad \varsigma_2 = \delta_2 + \gamma_2 + \mu, \quad \varsigma_3 = \epsilon + \delta_1 + \delta_2 + \mu,$$

$$\zeta_4 = \mu + \sigma_1, \quad \zeta_5 = \mu + \sigma_2, \quad \zeta_6 = \mu + \sigma_3.$$

Then the basic reproduction number from the product matrix $\mathcal{F}\mathcal{V}^{-1}$ is the maximum of the eigenvalues listed as follows:

$$\begin{aligned} \lambda_{1,2} &= \pm \sqrt{\frac{c^2 \rho_1 \beta_1 \Pi \Omega}{\mu \mu_{vd}^2 (\mu + \delta_1 + \gamma_1)}}, \\ \lambda_{3,4} &= \pm \frac{\alpha_1 \Pi \mu_{vl}^2 + \alpha_2 \rho_2 \Pi \Lambda}{\mu \mu_{vl}^2 (\mu + \delta_2 + \gamma_2)}, \\ \lambda_5 &= 0. \end{aligned}$$

Therefore, the basic reproduction number of the co-infection is given by

$$\mathcal{R}_0 = \max\{\mathcal{R}_{0d}, \mathcal{R}_{0l}\}. \tag{33}$$

3.3.5 Local stability of DFEP

Theorem 3.10 *DFEP is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.*

Proof The Jacobian matrix of the model at DFEP is obtained as follows:

$$\begin{pmatrix} -\mu & 0 & -\frac{\alpha_1 \Pi}{\mu} & -\frac{\alpha_1 \Pi}{\mu} & \sigma_1 & \sigma_2 & \sigma_3 & 0 & -\frac{c\beta_1 \Pi}{\mu} & 0 & -\frac{\alpha_2 \Pi}{\mu} \\ 0 & -\zeta_1 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{c\beta_1 \Pi}{\mu} & 0 & 0 \\ 0 & 0 & \frac{\alpha_1 \Pi}{\mu} - \zeta_2 & \frac{\alpha_1 \Pi}{\mu} & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\alpha_2 \Pi}{\mu} \\ 0 & 0 & 0 & -\zeta_3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_1 & 0 & \epsilon \eta & -\zeta_4 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_2 & \epsilon k(1 - \eta) & 0 & -\zeta_5 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & g & 0 & 0 & -\zeta_6 & 0 & 0 & 0 & 0 \\ 0 & -\frac{c\rho_1 \Omega}{\mu_{vd}} & 0 & 0 & 0 & 0 & 0 & -\mu_{vd} & 0 & 0 & 0 \\ 0 & \frac{c\rho_1 \zeta_2}{\mu_{vd}} & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_{vd} & 0 & 0 \\ 0 & 0 & -\frac{\rho_2 \Lambda}{\mu_{vl}} & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_{vl} & 0 \\ 0 & 0 & \frac{\rho_2 \Lambda}{\mu_{vl}} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_{vl} \end{pmatrix}. \tag{34}$$

From equation (34), we can get the following characteristic polynomial:

$$\begin{aligned} p(\lambda) &= [\lambda^2 + (\mu_{vd} + \zeta_1)\lambda + \mu_{vd}(1 - \mathcal{R}_{0d})] \left(\lambda^2 + \zeta_2 \left[1 + \frac{\mu_{vl}}{\mu \zeta_2} - \mathcal{R}_{0hl} \right] \lambda \right. \\ &\quad \left. + \mu_{vl} \zeta_2 (1 - \mathcal{R}_{0l})(\lambda + \zeta_4)(\lambda + \zeta_5)(\lambda + \zeta_6)(\lambda + \mu)(\lambda + \mu_{vd})(\lambda + \mu_{vl})(\lambda + \zeta_3) \right). \end{aligned}$$

Therefore, DFEP is locally asymptotically stable iff $\mathcal{R}_0 = \max\{\mathcal{R}_{0d}, \mathcal{R}_{0l}\} < 1$. □

3.3.6 Global stability of DFE

Theorem 3.11 *The equilibrium point $E_0 = (X^*, 0)$ of system (1) is globally asymptotically stable if $\mathcal{R}_0 \leq 1$ and conditions (i) and (ii) in the theorem [26] are satisfied.*

Proof We use the technique implemented by Castillo-Chavez and Song [26]. From equation (1), we can get $F(X, Z)$ and $G(X, Z)$, where $X = (S, R_d, R_l, R_{dl}, S_{vd}, S_{vl}) \in \mathcal{R}^6$ denotes

uninfected populations and $Z = (I_d, I_l, I_{dl}, I_{vd}, I_{vl}) \in \mathcal{R}^5$ denotes infected populations.

$$F(X, Z) = \begin{pmatrix} \Pi + \sigma_1 R_d + \sigma_2 R_l + \sigma_3 R_{dl} - [c\beta_1 I_{vd} + \alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu] S \\ \gamma_1 I_d + \varepsilon c I_{dl} - (\mu + \sigma_1) R_d \\ \gamma_2 I_l + \varepsilon k(1 - c) I_{dl} - (\mu + \sigma_2) R_l \\ g I_{dl} - (\mu + \sigma_3) R_{dl} \\ \Omega - c\rho_1 I_d S_{vd} - \mu_{vd} S_{vd} \\ \Lambda - \rho_2 I_l S_{vl} - \mu_{vl} S_{vl} \end{pmatrix}$$

and

$$G(X, Z) = \begin{pmatrix} c\beta_1 I_{vd} S - [\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl} + \mu + \delta_1 + \gamma_1] I_d \\ [\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl}] S - [c\beta_1 I_{vd} + \mu + \delta_2 + \gamma_2] I_l \\ [\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl}] I_d + \beta_1 I_{vd} I_l - (\varepsilon + \mu + \delta_1 + \delta_2) I_{dl} \\ c\rho_1 I_d S_{vd} - \mu_{vd} I_{vd} \\ \rho_2 I_l S_{vl} - \mu_{vl} I_{vl} \end{pmatrix}.$$

Now consider the reduced system $\frac{dX}{dt} = F(X, 0)$:

$$\frac{dX}{dt} = \begin{cases} \frac{dS}{dt} = \Pi - \mu S, \\ \frac{dS_{vd}}{dt} = \Omega - \mu_{vd} S_{vd}, \\ \frac{dS_{vl}}{dt} = \Lambda - \mu_{vl} S_{vl}. \end{cases} \tag{35}$$

$X^* = (\frac{\Pi}{\mu}, \frac{\Omega}{\mu_{vd}}, \frac{\Lambda}{\mu_{vl}})$ is a globally asymptotically stable equilibrium point for the reduced system $\frac{dX}{dt} = F(X, 0)$. This can be verified. From the solution of the first equation in equation (35) we obtain $S(t) = \frac{\Pi}{\mu} + (S(0) - \frac{\Pi}{\mu})e^{-\mu t}$, which approaches $\frac{\Pi}{\mu}$ as $t \rightarrow \infty$; and from the second and third equation of equation (35) we get $S_{vd} = \frac{\Omega}{\mu_{vd}} + (S_{vd}(0) - \frac{\Omega}{\mu_{vd}})e^{-\mu_{vd} t}$ and $S_{vl} = \frac{\Lambda}{\mu_{vl}} + (S_{vl}(0) - \frac{\Lambda}{\mu_{vl}})e^{-\mu_{vl} t}$, which approaches $\frac{\Omega}{\mu_{vd}}$ and $\frac{\Lambda}{\mu_{vl}}$ as $t \rightarrow \infty$. We note that this asymptotic dynamics is independent of the initial conditions in Ω , therefore the convergence of the solutions of the reduced system (35) is global in Ω . Now we compute

$$D_Z G(X^*, 0) = \begin{pmatrix} -\varsigma_1 & 0 & 0 & \frac{c\beta_1 \Pi}{\mu} & 0 \\ 0 & \frac{\alpha_1 \Pi}{\mu} - \varsigma_2 & \frac{\alpha_1 \Pi}{\mu} & 0 & \frac{\alpha_2 \Pi}{\mu} \\ 0 & 0 & -\varsigma_3 & 0 & 0 \\ \frac{c\rho_1 \Omega}{\mu_{vd}} & 0 & 0 & -\mu_{vd} & 0 \\ 0 & \frac{\rho_2 \Lambda}{\mu_{vl}} & 0 & 0 & -\mu_{vl} \end{pmatrix}.$$

Then $G(X, Z)$ can be written as

$$G(X, Z) = D_Z G(X^*, 0)Z - \hat{G}(X, Z),$$

and we want to show $\hat{G}(X; Z) \geq 0$, which is obtained as follows:

$$\hat{G}(X, Z) = \begin{pmatrix} \hat{G}_1(X, Z) \\ \hat{G}_2(X, Z) \\ \hat{G}_3(X, Z) \\ \hat{G}_4(X, Z) \\ \hat{G}_5(X, Z) \end{pmatrix} = \begin{pmatrix} c\beta_1(\frac{\Pi}{\mu} - S)I_{vd} + [\alpha_1(I_l + I_{dl}) + \alpha_2 I_{vl}]I_d \\ \alpha_1(\frac{\Pi}{\mu} - S)I_l + \alpha_1(\frac{\Pi}{\mu} - S)I_{dl} + \alpha_2(\frac{\Pi}{\mu} - S)I_{vl} + \beta_1 I_{vd}I_l \\ -(\alpha_1(I_l + I_{dl})I_d + \alpha_2 I_{vl}I_d + \beta_1 I_{vd}I_l) \\ c\rho_1(\frac{\Omega}{\mu_{vd}} - S_{vd})I_d \\ \rho_2(\frac{\Lambda}{\mu_{vl}} - S_{vl})I_l \end{pmatrix}. \tag{36}$$

In equation (36), $\hat{G}_3(X, Z) < 0$, which leads to $\hat{G}(X, Z) < 0$ for all $(X, Z) \in \Omega$. Therefore, this proves that DFEP may not be globally asymptotically stable when $\mathcal{R}_0 < 1$. Hence the endemic equilibrium point coexists with DFEP when $\mathcal{R}_0 < 1$. This implies that the model exhibits backward bifurcation at $\mathcal{R}_0 = 1$. \square

3.4 Sensitivity analysis

Sensitivity is performed to identify the most dominant parameters for the spreading out as well as control of infection in the community. To go through sensitivity analysis, we follow the technique described in [27]. The sensitivity index of \mathcal{R}_0 with respect to a parameter, say y , is given by

$$A_y^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial y} \times \frac{y}{\mathcal{R}_0}.$$

Since $\mathcal{R}_0 = \max\{\mathcal{R}_{0d}, \mathcal{R}_{0l}\}$, we obtain the sensitivity analysis of \mathcal{R}_{0d} and \mathcal{R}_{0l} separately in the following way:

$$\begin{aligned} A_\beta^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \beta} \times \frac{\beta}{\mathfrak{R}_{0d}} = \frac{\rho_1 \Omega \Pi}{2\mathfrak{R}_{0d} \mu_{vd}^2 (\delta_1 + \gamma_1 + \mu) \mu} \frac{\beta}{\mathfrak{R}_{0d}} = \frac{1}{2} \geq 0, \\ A_{\rho_1}^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \rho_1} \times \frac{\rho_1}{\mathfrak{R}_{0d}} = \frac{\beta \Omega \Pi}{2\mathfrak{R}_{0d} \mu_{vd}^2 (\delta_1 + \gamma_1 + \mu) \mu} \frac{\rho_1}{\mathfrak{R}_{0d}} = \frac{1}{2} \geq 0, \\ A_c^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial c} \times \frac{c}{\mathfrak{R}_{0d}} = 1 > 0, \\ A_{\delta_1}^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \delta_1} \times \frac{\delta_1}{\mathfrak{R}_{0d}} = -\frac{\delta_1}{2(\delta_1 + \gamma_1 + \mu)} < 0, \\ A_{\gamma_1}^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \gamma_1} \times \frac{\gamma_1}{\mathfrak{R}_{0d}} = -\frac{\gamma_1}{2(\delta_1 + \gamma_1 + \mu)} < 0, \\ A_\mu^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \mu} \times \frac{\mu}{\mathfrak{R}_{0d}} = -\frac{\delta_1 + \gamma_1 + 2\mu}{2(\delta_1 + \gamma_1 + \mu)} < 0, \\ A_{\mu_{vd}}^{\mathfrak{R}_{0d}} &= \frac{\partial \mathfrak{R}_{0d}}{\partial \mu_{vd}} \times \frac{\mu_{vd}}{\mathfrak{R}_{0d}} = -1 < 0, \\ A_{\alpha_1}^{\mathfrak{R}_{0l}} &= \frac{\partial \mathfrak{R}_{0l}}{\partial \alpha_1} \times \frac{\alpha_1}{\mathfrak{R}_{0l}} = \frac{\alpha_1 \mu_{vl}^2 \Pi}{\alpha_2 \rho_2 \Pi \Lambda + \alpha_1 \Pi \mu_{vl}^2} > 0, \\ A_{\alpha_2}^{\mathfrak{R}_{0l}} &= \frac{\partial \mathfrak{R}_{0l}}{\partial \alpha_2} \times \frac{\alpha_2}{\mathfrak{R}_{0l}} = \frac{\Lambda \Pi \rho_2 \alpha_2}{\alpha_2 \rho_2 \Pi \Lambda + \alpha_1 \Pi \mu_{vl}^2} > 0, \\ A_{\rho_2}^{\mathfrak{R}_{0l}} &= \frac{\partial \mathfrak{R}_{0l}}{\partial \rho_2} \times \frac{\rho_2}{\mathfrak{R}_{0l}} = \frac{\Lambda \Pi \rho_2 \alpha_2}{\alpha_2 \rho_2 \Pi \Lambda + \alpha_1 \Pi \mu_{vl}^2} > 0, \\ A_{\delta_2}^{\mathfrak{R}_{0l}} &= \frac{\partial \mathfrak{R}_{0l}}{\partial \delta_2} \times \frac{\delta_2}{\mathfrak{R}_{0l}} = -\frac{\delta_2}{\delta_2 + \gamma_2 + \mu} < 0, \end{aligned}$$

Table 2 Sensitivity indices table

Parameter symbol	Sensitivity indices
\mathfrak{R}_{0d}	Basic reproduction number of dengue
β	+ve
ρ_1	+ve
c	+ve
δ_1	-ve
γ_1	-ve
μ	-ve
μ_{vd}	-ve
\mathfrak{R}_{0l}	Basic reproduction number of leptospirosis
α_1	+ve
α_2	+ve
ρ_2	+ve
δ_2	-ve
γ_2	-ve
μ	-ve
μ_{vl}	-ve

$$A_{\gamma_2}^{\mathfrak{R}_{0l}} = \frac{\partial \mathfrak{R}_{0l}}{\partial \gamma_2} \times \frac{\gamma_2}{\mathfrak{R}_{0l}} = -\frac{\gamma_2}{\delta_2 + \gamma_2 + \mu} < 0,$$

$$A_{\mu}^{\mathfrak{R}_{0l}} = \frac{\partial \mathfrak{R}_{0l}}{\partial \mu} \times \frac{\mu}{\mathfrak{R}_{0l}} = -\frac{2\mu + \delta_2 + \gamma_2}{\delta_2 + \gamma_2 + \mu} < 0,$$

$$A_{\mu_{vd}}^{\mathfrak{R}_{0l}} = \frac{\partial \mathfrak{R}_{0l}}{\partial \mu_{vd}} \times \frac{\mu_{vd}}{\mathfrak{R}_{0l}} = -\frac{2\alpha_2 \rho_2 \Pi \Lambda}{\alpha_2 \rho_2 \Pi \Lambda + \alpha_1 \mu_{vl}^2} < 0.$$

The above computation of sensitivity analysis is summarized in Table 2.

From Table 2, we understand that the parameters with positive sensitivity indices, particularly β_1 , ρ_1 , c , α_1 , α_2 , and ρ_2 , have great potential in expanding dengue, leptospirosis, and their co-infection in the community. However, the parameters with negative indices, particularly δ_1 , γ_1 , δ_2 , γ_2 , μ , μ_{vd} , and μ_{vl} , have a great contribution in controlling the expansion of dengue, leptospirosis, and their co-infection in the community if their values are increased. From this policy makers and stakeholders are expected to act accordingly in combating dengue, leptospirosis, and their co-infection in the community.

4 Numerical simulations

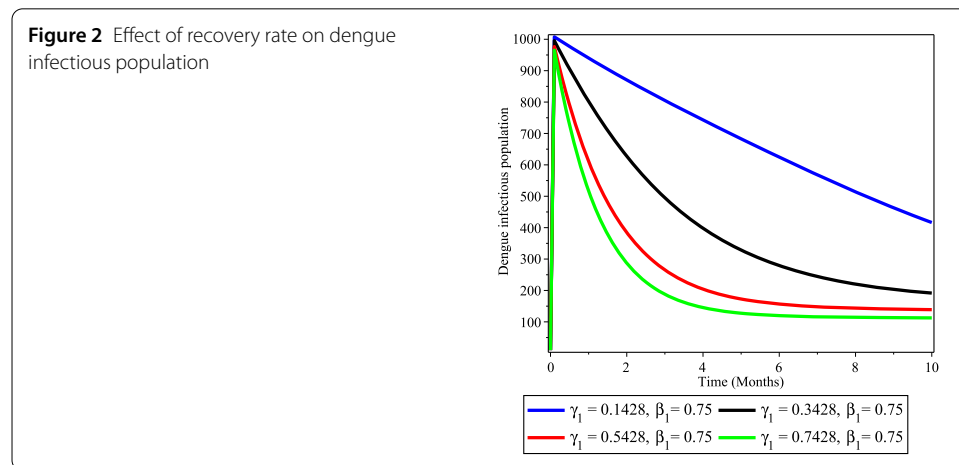
Analytical results cannot be complete without numerical result verification. In this section, the full dengue–leptospirosis co-infection model numerical simulation is performed using Maple 18. The simulation is used for checking the effect of some parameters in the expansion as well as the control of dengue only, leptospirosis only, and co-infection of dengue and leptospirosis. For simulation purpose the parameter values in Table 3 are used.

4.1 Effect of recovery rate (γ_1) on dengue infectious population

In Fig. 2, we experimented with the effect of γ_1 in reducing dengue-only infectious population by maintaining the contact rate (β_1) constant. The figure reflects that when the values of γ_1 increase, the number of dengue only infectious population is going down. From this we should concentrate on improving recovery rates either by treating infected populations or by raising individuals’ immunity levels to dengue disease in the population. It should be viewed by policy makers as a mitigation strategy.

Table 3 Parameter values for the dengue leptospirosis co-infection model

Parameter symbol	Value day^{-1}	Source
Π	2.0	Assumed
β_1	0.75	[11, 12]
α_1	0.04	[19, 28]
α_2	0.04	[19, 28]
δ_1	0.0015	[12]
δ_2	0.003	[19, 28]
σ_1	0.0027	Assumed
σ_2	0.00285	[19, 28]
σ_3	0.002	Assumed
ρ_1	0.75	[11, 12]
ρ_2	0.04	[19, 28]
γ_1	0.1428	[12]
γ_2	0.0027	[19, 28]
μ	0.0000128	[11, 12]
Λ	2.3	Assumed
Ω	2.5	Assumed
μ_{vd}	0.071	[11, 12]
μ_{vl}	0.0018	[19, 28]
c	0.5	[12]

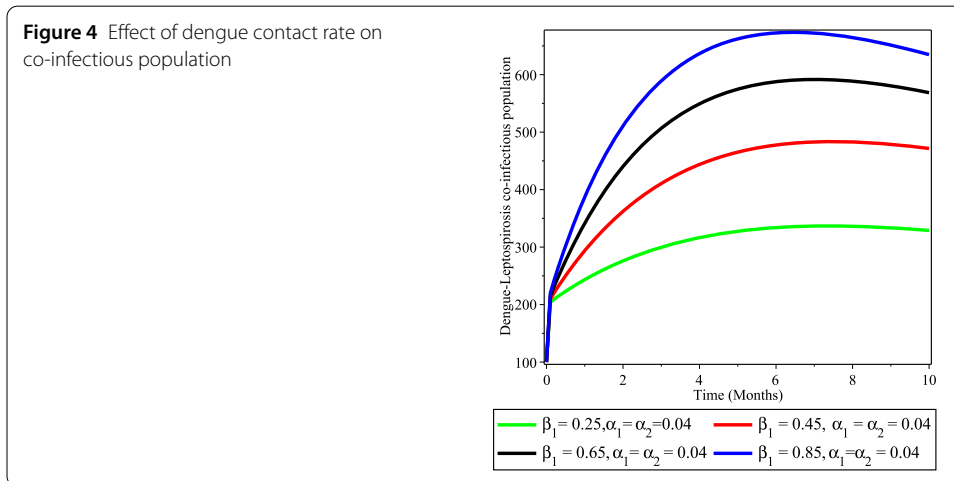
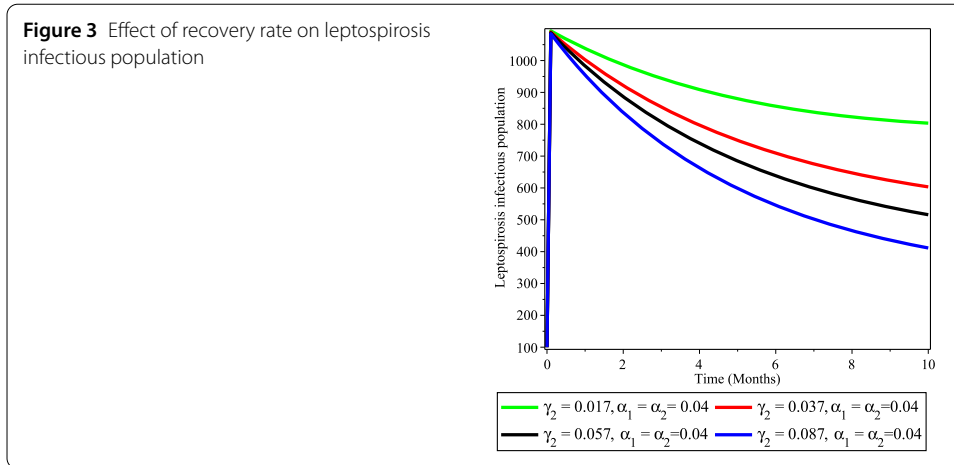


4.2 Effect of recovery rate (γ_2) on leptospirosis infectious population

In Fig. 3, it is shown that γ_2 plays a significant role in bringing down the leptospirosis infection. When the value of γ_2 increased from 0.017 to 0.087, the amount of infectious population due to leptospirosis decreased, where the contact rate is kept constant, which is $\alpha_1 = \alpha_2$. It can also be used by policy makers as a tool for mitigation.

4.3 Effect of dengue contact rate (β_1) on co-infectious population

As it is shown in Fig. 4, the contact rate of leptospirosis ($\alpha_1 = \alpha_2$) and the recovery rate of co-infectious population (ε) are kept constant. The figure reflects that as the value of contact rate of dengue increased, the co-infectious population increased, which means increased expansion of co-infection. From this we can see that decreasing of the dengue contact rate is significant in the controlling of co-infection transmission. Therefore, stakeholders are expected to work on decreasing the contact rate of susceptible humans and dengue vector by using either bednet or chemical or using an appropriate method of prevention mechanism to bring down the expansion of co-infection in the community.

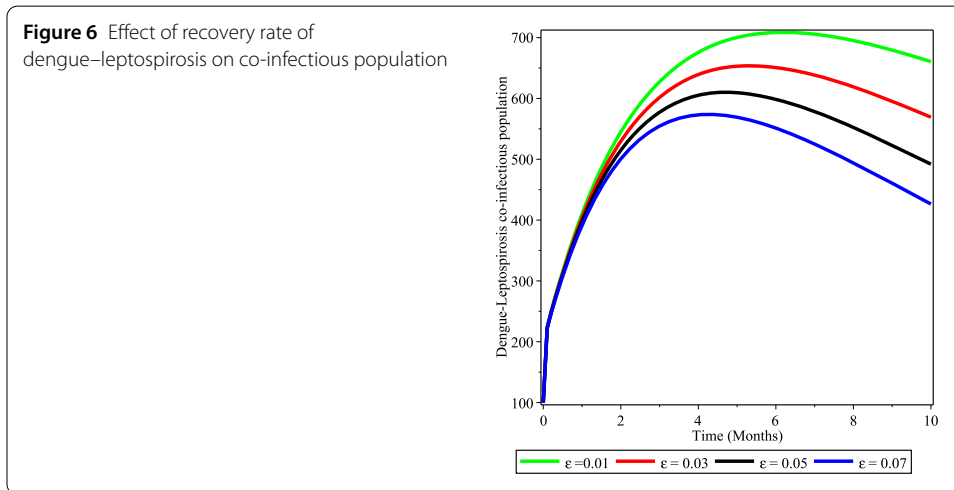
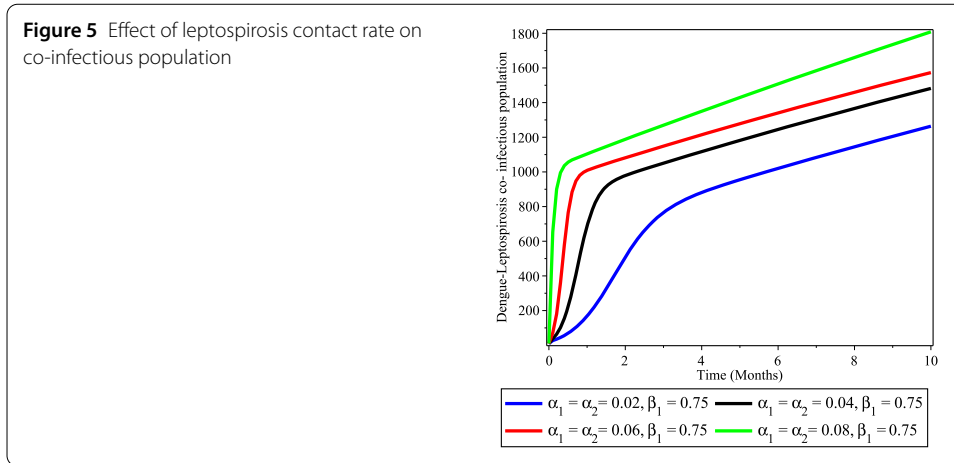


4.4 Effect of leptospirosis contact rate (α_1 and α_2) on co-infectious population

Similarly, we investigated the effect of leptospirosis contact rate ($\alpha_1 = \alpha_2$) in the expansion of dengue–leptospirosis co-infection while keeping the recovery rate of co-infection (ε) constant. Figure 5 shows that co-infectious population decreases as the leptospirosis contact rate is decreasing, by keeping dengue contact rate (β_1) and (ε) constant. This implies that, in order to mitigate the co-infection, it is advisable to reduce the rate of contact with infectious humans, and that the host vector of leptospirosis is crucial.

4.5 Effect of recovery rate of dengue–leptospirosis (ε) on co-infectious population

Here, we experimented on the effect of recovery rate of dengue and leptospirosis (ε) on the co-infectious population. As we explained in the model description, due to treatment or other mechanisms, co-infectious population either recover from dengue only or from leptospirosis only or from both diseases with their own probability and join their respective recovered compartment. Therefore, Fig. 6 shows that increasing the rate of recovery of the co-infectious population has a great advantage in reducing both diseases in the population.



5 Conclusions

The deterministic co-infection model for dengue-leptospirosis disease was developed using ordinary differential equations, and the population is subdivided into eleven compartments. The qualitative analysis of the model was done by splitting the full model into two, which are dengue only and leptospirosis only models. The analysis of the model shows that there exists a region where the model is mathematically and epidemiologically well posed. Basic reproduction numbers, disease-free equilibrium, endemic equilibria, stability analysis of equilibrium points, and sensitivity analysis of basic reproduction of dengue only, leptospirosis only, and the full model were analyzed in their respective order. Numerically, we experimented on the effect of basic parameters in the expansion or control of dengue only, leptospirosis only, and co-infectious diseases. From the result, we conclude that an increase in the rate of dengue recovery contributes greatly to reducing dengue infection in the community. Similarly, increasing the recovery rate for leptospirosis also contributes to the reduction of leptospirosis. The rate of recovery for co-infection also has an effect on reducing co-infectious population if its value has been increased. The other finding obtained in this section is that decreasing either dengue or leptospirosis contact rate has a great influence on controlling co-infection of dengue and leptospirosis in the population.

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The data supporting this deterministic model are from previously published articles.

Competing interests

The author declares that he has no competing interests.

Authors' contributions

All of this work was done by HTA. The author read and approved the final manuscript.

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