Effect of active case finding on dengue control: Implications from a mathematical model

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Abstract

Dengue control in India is a challenging task due to complex healthcare settings. In yesteryears, an amplification of dengue infections in India posed the need for introspection of existing dengue control policies. Prior understanding of the impacts of control interventions is necessary for their future implementation. In this paper, we propose and analyze a compartmental model of dengue to assess the impact of active case finding (ACF) on dengue disease transmission. Currently, primary prevention of dengue is possible only with vector control and personal protection from the bites of infected mosquitoes. Although a few experimental studies are performed to assess ACF in dengue disease, but this is the first attempt to represent and study the dynamics of disease using ACF as a control strategy. Local and global dynamics of the system are studied. We use sensitivity analysis to see the effects of controllable parameters of the model on the basic reproduction number and total number of infective population. We find that decrease in the biting rate of mosquitoes, and increase in the rate of hospitalization and/or notification, death rate of mosquitoes and ACF for asymptomatic and symptomatic individuals play crucial role for the reduction of disease prevalence. We calibrate our model to the yearly dengue cases in eight dengue endemic states of India. The results of our study show that ACF of symptomatic individuals will have significant effect on dengue case reduction but ACF of asymptomatic individuals cannot be ignored. Our findings indicate that the healthcare organizations must focus on ACF of symptomatic as well as asymptomatic individuals along with personal protection and mosquitoes control to achieve rapid reduction of dengue cases in India.

Key words: Dengue, Epidemic model, Active case finding, Sensitivity analysis, Parameter estimation.

1. Introduction

Dengue fever is a vector borne disease, transmitted by the bite of Aedes aegypti or Aedes albopictus female mosquitoes, distributed mainly in tropical and subtropical areas and is caused by four closely related dengue serotypes (DENV 1-4) [1, 2]. Almost all age groups can be affected by dengue. Its symptoms become apparent after 3-14 days of the bite of infected mosquito [3]. After recovery from one serotype of dengue, one can become immune to that particular serotype, but is prone to get infection with the remaining three serotypes [4]. In recent years, the rate of dengue cases is accelerating and figures from World Health Organization confirm 284–528 million cases per year around the globe [5]. Unfortunately, no effective vaccine is available against dengue fever [6], but there are numerous candidate vaccines (such as, inactivated whole virus vaccines, live attenuated mono and tetravalent formulation).
and recombinant subunit vaccines), undergoing clinical trials in various phases [7, 8, 9, 10, 11]. Thus, in order to avoid dengue infection, people have to prevent themselves from the mosquitoes. Use of insecticide, removal of mosquito breeding sites generated by humans in households (e.g., old toys, water containers, and tires) and making people aware about mosquito net and other mosquito repeller are some useful ways for controlling the disease [5, 12]. However, these methods are not sufficiently effective due to frequent outbreaks of the disease in some areas. In such scenarios, mathematical models of vector-borne diseases include ideas of how to curb the disease.

After the seminal work of Fischer and Halstead [13], research on dengue transmission has gained commendable attention. In most of the studies, effect of epidemiological interactions between multiple dengue serotypes has been studied. Feng et al. [14] examined the principle of competitive exclusion in a dengue model consisting of two serotypes. Using spatial epidemic data, basic reproduction number for a dengue model was estimated by Chowell et al. [15]. Tewa et al. [16] studied a dengue model by considering one type of virus. Using Lyapunov functions, they have shown global asymptotic stability of disease-free and endemic equilibria. Garba et al. [17] developed and rigorously analyzed a compartmental model for spread and control of dengue disease. They considered transmission by exposed humans and mosquitoes as well. They showed that the model exhibits the phenomenon of backward bifurcation when standard incidence is considered. Further, they have shown that taking into account mass-action incidence function, no backward-bifurcation can be observed. Derouich et al. [18] have shown that employing environment management or chemical methods for prevention of dengue is not sufficient; it can only delay the outbreak of the disease. Influence of spatial heterogeneity on the disease emergence has been explored by Favier et al. [19]. Some stochastic models for dengue infection are also available in literature [20, 21, 22]. Degallier et al. [23] and Kongnuy et al. [24] have investigated the dynamics of dengue by using statistical methods. Using numerical techniques, Perez et al. [25] investigated the dynamics of dengue disease. Some mathematical models have been studied for dynamics and control of dengue infection [15, 17, 26, 27, 28]. In some models, optimal control theory is used to design the paths to limit the spread of dengue [29, 30].

To the best of our knowledge, the aforementioned studies have focused on mosquito control and personal protection as preventive measures, but didn’t attempt to assess the impact of active case finding as a control measure for the dengue epidemic. Active case finding (ACF) requires a special effort by the healthcare organizations to increase the detection of dengue in a given population. This strategy identifies and brings into treatment people with dengue who have not sought diagnostic services themselves. ACF can reduce the number of subsequent dengue infections and prevent secondary cases by detecting and treating patients on the early stage of infection. ACF is conducted by trained healthcare agents who make face-to-face contact with patients and immediately prescribes onsite evaluation [31, 32, 33, 34]. Moreover, ACF can be used to fill the data gaps caused by under reporting of dengue cases. A community-based active dengue fever surveillance among the individuals of age group 0–19 years has been conducted by Vong et al. [35]. The surveillance is done in rural and urban areas of Cambodia, Kampong Cham, during 2006-2008. The main purpose of surveillance was to estimate the true burden of dengue in the area. As a result of this surveillance, a higher disease incidence was found than that reported to the national surveillance system. Moreover, the incidence of disease was found to be high in both rural and urban areas, especially in preschool children. In a more recent study [36], authors attempted to quantify the proportion of asymptomatic dengue infection in some regions of Delhi. They tested a total of 2,125 persons, with or without symptoms of dengue and found relatively high prevalence of asymptomatic cases to that of symptomatic cases. Further, symptomatic dengue patients were referred to nearby hospitals for medications while cases with asymptomatic infections were provided necessary knowledge about subsequent secondary infections. This study is somehow similar in nature to that of
ACF. Thus, ACF can be helpful to reduce dengue burden in two ways: it will fill the data gaps caused by under-reporting and simultaneously detection of dengue patients in early stage will prevent secondary infections. This twofold benefits of ACF motivated us to investigate its impact on dengue control. As far our knowledge goes, this is the first attempt to represent the dengue dynamics mathematically using ACF as a control strategy.

For case study, we consider dengue prevalence during 2007–2017 in eight dengue endemic states of India, namely: Kerala, Delhi, Gujarat, West Bengal, Andhra Pradesh, Rajasthan, Maharashtra and Karnataka. In India, the dengue haemorrhage fever/dengue shock syndrome (DHF/DSS) occurred in various parts of the country since 1988 and major outbreak was occurred around Delhi and Lucknow in the year 1996 [37]. India experienced significantly high levels of dengue cases during last two decades [38]. In 2018, a provisional total of 14,233 dengue cases (with 30 deaths) has been reported in India till 22nd July [39]. In order to stop the rising number of dengue cases, the government of India has launched a major campaign to enhance awareness among people about methods of prevention. Despite the use of various methods for the control of mosquitoes and personal protections by people themselves, dengue is still not under control in most of the states.

Remainder of the paper is presented in the following way: Section 2 contains model formulation and underlying assumptions. Dynamics of disease-free equilibrium is studied in Section 3. We analyze the system for feasibility and stability of endemic equilibrium in Section 4. Sensitivity analysis is performed in Section 5. We calibrate our model for yearly dengue case data of eight different states of India in Section 6. In Section 7, we study the impacts of ACF on dengue burden in these states. The paper ends with discussion and conclusion in Section 8.

2. Model formulation

At any time $t > 0$, the total mosquito population ($N_v$) is sub-divided into three classes: susceptible mosquitoes ($S_v$), mosquitoes exposed to the dengue virus ($E_v$) and infected mosquitoes ($I_v$). We divide the total human population ($N_h$) into seven sub-classes: high risk susceptible individuals ($S_{h1}$), low risk susceptible individuals ($S_{h2}$), individuals exposed to dengue virus ($E_h$), asymptomatic individuals ($A_h$), individuals with dengue symptoms ($I_h$), hospitalized and/or notified individuals ($P_h$) and recovered individuals ($R_h$). Symptomatic dengue infection is referred to fever with at least two symptoms of dengue (headache, retro-ocular pain, arthralgia, myalgia, rash) while asymptomatic dengue infection is defined as no clinical symptoms of dengue as in the case of symptomatic infection [5]. The individuals in the $P_h$ class are assumed be those who are admitted to the hospital and the people who are notified as confirmed dengue patients.

Susceptible mosquitoes are assumed to be recruited at a constant rate $\pi_v$. They move to the exposed class by acquiring dengue through contacts with infected humans (asymptomatic and symptomatic). We consider standard incidence for the interactions between susceptible mosquitoes and infected humans. Exposed mosquitoes are assumed to move to the infected class at a rate $\gamma_v$. Mosquitoes in each class are assumed to die from natural causes at a rate $\mu_v$. Recovered class is not considered for the mosquito population. The reason behind this is once infected from dengue virus, the female mosquitoes remain infected throughout their life span [40].

The individuals are recruited in the region at a constant rate $\pi_h$ (by birth or immigration) and assumed to join the susceptible class. A fraction $r$ of total newly recruited populations join the high risk susceptible population ($S_{h1}$) and the remaining join the low risk susceptible population ($S_{h2}$). Individuals in classes $S_{h1}$ and $S_{h2}$ are assumed to join the exposed class on effective contact with infected mosquitoes. The interactions between susceptible humans and infected mosquitoes are assumed to be of standard incidence type. The individuals in class $S_{h2}$ are assumed to contract the disease at a lower rate than the
individuals in class $S_h$. The exposed humans are assumed to move in the infected class at a rate $\gamma_h$, a fraction $\rho$ of which join the asymptomatic class $A_h$, while the remaining ones join the symptomatic class $I_h$. The individuals in the symptomatic class are hospitalized and/or notified at a constant rate $\eta$. The individuals in classes $A_h$, $I_h$ and $P_h$ are assumed to recover from the disease at the rates $q_1$, $q_2$ and $q_3$, respectively. The natural death of individuals in each class is assumed to be at a constant rate $\mu_h$. Furthermore, the asymptomatic and symptomatic individuals are notified through ACF at constant rates $p_1$ and $p_2$, respectively. The recovered individuals do not acquire the infection again as they get lifelong immunity. We assumed that the hospitalized and/or notified individuals are not going to infect others because they will be kept in mosquito-free environments.

The compartmental flow diagram is depicted in Fig. 1. Keeping the above assumptions in mind, we
developed the following mathematical model for the transmission dynamics of dengue:

\[
\begin{align*}
\frac{dS_v}{dt} &= \pi_v - \beta \alpha_h S_v \left( \frac{I_h + \lambda A_h}{N_h} \right) - \mu_v S_v, \\
\frac{dE_v}{dt} &= \beta \alpha_h S_v \left( \frac{I_h + \lambda A_h}{N_h} \right) - (\gamma_v + \mu_v) E_v, \\
\frac{dI_v}{dt} &= \gamma_v E_v - \mu_v I_v, \\
\frac{dS_h}{dt} &= r\pi_h - \beta \alpha_v I_v \left( \frac{S_h}{N_h} \right) - \mu_h S_h, \\
\frac{dS_{h1}}{dt} &= (1 - r)\pi_h - \beta \theta \alpha_v I_v \left( \frac{S_{h2}}{N_h} \right) - \mu_h S_{h1}, \\
\frac{dS_{h2}}{dt} &= (1 - r)\pi_h - \beta \theta \alpha_v I_v \left( \frac{S_{h1}}{N_h} \right) - \mu_h S_{h2}, \\
\frac{dE_h}{dt} &= \beta \alpha_v I_v \left( \frac{S_{h1} + \theta S_{h2}}{N_h} \right) - (\gamma_h + \mu_h) E_h, \\
\frac{dA_h}{dt} &= \rho \gamma_h E_h - (\mu_h + q_1 + p_1) A_h, \\
\frac{dI_h}{dt} &= (1 - \rho)\gamma_h E_h - (\mu_h + \eta + q_2 + p_2) I_h, \\
\frac{dP_h}{dt} &= p_1 A_h + (\eta + p_2) I_h - (q_3 + \mu_h + \delta) P_h, \\
\frac{dR_h}{dt} &= q_1 A_h + q_2 I_h + q_3 P_h - \mu_h R_h.
\end{align*}
\]

(2.1)

All parameters involved in the system (2.1) are assumed to be positive and also the initial conditions are taken to be positive values. The biological meanings of variables and parameters involved in the system (2.1) are given in Tables 1 and 2, respectively.

| Variables | Descriptions |
|-----------|--------------|
| $S_v$     | Number of susceptible mosquito population |
| $E_v$     | Number of exposed mosquito population |
| $I_v$     | Number of infected mosquito population |
| $S_{h1}$  | Number of high risk susceptible human population |
| $S_{h2}$  | Number of low risk susceptible human population |
| $E_h$     | Number of exposed human population |
| $A_h$     | Number of asymptomatic human population |
| $I_h$     | Number of symptomatic human population |
| $P_h$     | Number of hospitalized and/or notified human population |
| $R_h$     | Number of recovered human population |

It is worth noting that the feasible region for system (2.1) is given in the following lemma [41, 42].

**Lemma 2.1.** The region of attraction for all solutions initiating in the positive orthant is given by the set $\Omega$:

\[
\Omega = \{ (N_v, S_{h1}, S_{h2}, N_h) : 0 \leq N_v(t) \leq Z_1, 0 \leq S_{h1} \leq Z_2, 0 \leq S_{h2} \leq Z_3, 0 \leq N_h \leq Z_4 \},
\]

(2.2)
| Parameters | Descriptions                                                                 | Units     | Values     |
|------------|------------------------------------------------------------------------------|-----------|------------|
| $\pi_v$    | Recruitment rate of adult susceptible mosquito population                     | year$^{-1}$ | 350000    |
| $\beta$    | Average biting rate per mosquito per person                                   | year$^{-1}$ | Estimated  |
| $\alpha_h$ | Transmission probability from infected human to susceptible mosquito         | —         | 0.75      |
| $\lambda$  | Relative infectiousness of asymptomatic humans in relation to symptomatic humans | —         | 0.5       |
| $\mu_v$    | Natural death rate of adult mosquito population                               | year$^{-1}$ | 3         |
| $\gamma_v$ | Intrinsic incubation                                                         | year$^{-1}$ | 3.795     |
| $\pi_h$    | Recruitment rate of susceptible human                                          | year$^{-1}$ | 273600    |
| $\rho$     | Fraction of newly recruited individuals joining the high risk susceptible class| —         | 0.25      |
| $\alpha_v$ | Transmission probability from infected mosquito to susceptible human         | —         | 0.75      |
| $\mu_h$    | Natural death rate of human                                                   | year$^{-1}$ | 0.0154    |
| $\gamma_h$ | Extrinsic incubation                                                         | year$^{-1}$ | 3.3       |
| $\theta$   | Relative chance of infection of low risk susceptible in relation to high risk susceptible | —         | 0.5       |
| $\rho$     | Fraction of exposed human population joining the asymptomatic class          | —         | 0.75      |
| $p_1$      | Active case finding rate of asymptomatic class                               | year$^{-1}$ | Varied    |
| $p_2$      | Active case finding rate of symptomatic class                                | year$^{-1}$ | Varied    |
| $\eta$     | Rate of hospitalization and/or notification of symptomatic human             | year$^{-1}$ | Estimated |
| $q_1$      | Natural recovery rate of asymptomatic human                                  | year$^{-1}$ | 4         |
| $q_2$      | Natural recovery rate of symptomatic human                                   | year$^{-1}$ | 0.0355    |
| $q_3$      | Recovery rate of hospitalized and/or notified human                          | year$^{-1}$ | 4.5972    |
| $\delta$   | Disease related death rate of human                                           | year$^{-1}$ | 0.0001    |
where

\[
\begin{align*}
Z_1 &= \max \left\{ \frac{\pi_v}{\mu_v}, N_v(0) \right\}, \quad Z_2 = \max \left\{ \frac{r\pi_h}{\mu_h}, S_{h1}(0) \right\}, \quad Z_3 = \max \left\{ \frac{(1-r)\pi_h}{\mu_h}, S_{h2}(0) \right\}, \\
Z_4 &= \max \left\{ \frac{\pi_h}{\mu_h}, N_h(0) \right\}, \quad Z_5 = \min \left\{ \frac{\pi_h}{\mu_h + \delta}, N_h(0) \right\},
\end{align*}
\]

which is compact and invariant with respect to system (2.1).

For proof of this lemma, see Appendix A.

We first analyze the system through its equilibrium points. Equilibrium points are the values of \( S_v, E_v, I_v, S_{h1}, S_{h2}, E_h, A_h, I_h, P_h \) and \( R_h \) that remain constant over time. The equilibrium points of system (2.1) can be obtained by equating the derivatives to zero.

3. Disease-free equilibrium and its stability

The disease-free equilibrium of the system (2.1) is \( E_0 = \left( \frac{\pi_v}{\mu_v}, 0, 0, \frac{r\pi_h}{\mu_h}, (1-r)\pi_h, 0, 0, 0, 0 \right) \), which is always feasible. Local stability of the equilibrium \( E_0 \) can be established in terms of the basic reproduction number \( (R_0) \), a potential measure which determine that a disease invade a population.

3.1. Basic reproduction number

Using next-generation operator method [43], we determine the expression for basic reproduction number. For this, we find the matrices \( F \) (of new infection terms) and \( V \) (of the transition terms), as follows:

\[
F = \begin{pmatrix}
0 & 0 & 0 & \beta \alpha h \mu_1 \pi_v & \beta \alpha h \mu_1 \pi_v & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & \beta \alpha v \[r + \theta (1-r)] & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix},
\]

\[
V = \begin{pmatrix}
\gamma_v + \mu_v & 0 & 0 & 0 & 0 & 0 \\
-\gamma_v & \mu_v & 0 & 0 & 0 & 0 \\
0 & 0 & \gamma_h + \mu_h & 0 & 0 & 0 \\
0 & 0 & -r \gamma_h & \mu_h + q_1 + q_2 & 0 & 0 \\
0 & 0 & 0 & 0 & \mu_h + \eta + q_2 + p_2 & 0 \\
0 & 0 & 0 & -p_1 & -\eta = p_2 & q_3 + \mu_h + \delta 
\end{pmatrix}.
\]

The basic reproduction number is given by \( R_0 = \rho(FV^{-1}) \), where \( \rho \) is the spectral radius of the next-generation matrix \((FV^{-1})\). Thus, from the model (2.1), we obtain the expression for \( R_0 \) as

\[
R_0^2 = \frac{\beta^2 \pi_v \alpha h \mu_h \gamma_v \gamma_h \{r + \theta (1-r)\}}{\mu_v \mu_h (\gamma_v + \mu_v)(\gamma_h + \mu_h)} \left[ \frac{\lambda \rho}{\mu_h + q_1 + p_1} + \frac{1 - \rho}{\eta + \mu_h + q_2 + p_2} \right]. \tag{3.1}
\]

The quantity \( R_0 \) is known as “basic reproduction number, the expected number of secondary cases produced in completely susceptible population, by a typical infective individual” for the system (2.1). From the expression of \( R_0 \), the role of active case finding for asymptomatic as well as symptomatic individuals on the disease prevalence are evident. It is to be noted that by increasing the rate of hospitalization and/or notification of symptomatic humans and active case finding of asymptomatic and symptomatic individuals, the values of \( R_0 \) decreases. The parameters \( \beta \) and \( \mu_v \) appear in square terms
and hence affects the values of $R_0$ significantly. The former increases the values of $R_0$ while the latter decreases the values of $R_0$.

Following [43], regarding local stability of the disease-free equilibrium $E_0$ of the system (2.1), we have the following theorem.

**Theorem 3.1.** For system (2.1), the disease-free equilibrium $E_0$ is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

For proof of this theorem, see Appendix B.

**Remark 3.1.** The above theorem imply that whenever $R_0$ is less than unity, a small influx of infected mosquitoes/humans into the community would not generate large outbreaks, and the disease dies out in time.

4. **Endemic equilibrium and its stability**

4.1. **Existence of endemic equilibrium**

For model (2.1), an endemic equilibrium is $E^\ast = (S^\ast_v, E^\ast_v, I^\ast_v, S^\ast_h, A^\ast_h, E^\ast_h, R^\ast_h)$, whose components are positive solutions of equilibrium equations of the system (2.1).

We define a new variable $Q$ as

$$Q = \beta_0 \frac{I^*_v}{N^*_h}. \quad (4.1)$$

From the equilibrium equations of system (2.1), we have

$$S_v^* = \frac{\pi_v}{\mu_v + \beta_0 h \left( \frac{I^*_v + \Lambda^*_h}{N^*_h} \right)},$$

$$I_v^* = \frac{\beta_0 h \gamma_v \pi_v}{\mu_v(\gamma_v + \mu_v)} \left( \frac{I^*_v + \Lambda^*_h}{N^*_h} \right),$$

$$S_h^* = \frac{(1 - r) \pi_h}{\theta Q + \mu_h},$$

$$A_h^* = \frac{\rho r h E^*_h}{\mu_h + q_2 + p_2},$$

$$P_h^* = \frac{\gamma h E^*_h}{\mu_h + \delta + q_3} \left( \frac{p_1 \rho}{\mu_h + q_1 + p_1} + \frac{(1 - \rho)(\eta + p_2)}{\mu_h + \eta + q_2 + p_2} \right),$$

$$R_h^* = \frac{q_1 A^*_h + q_2 I^*_h + q_3 P^*_h}{\mu_h}.$$

(4.2)

The total human population is given by

$$N^*_h = \frac{1}{\mu_h} \left[ \pi_h - \frac{\delta \gamma h E^*_h}{\mu_h + \delta + q_3} \left( \frac{p_1 \rho}{\mu_h + q_1 + p_1} + \frac{(1 - \rho)(\eta + p_2)}{\mu_h + \eta + q_2 + p_2} \right) \right]. \quad (4.3)$$

Now, using equations (4.2) and (4.3) in equation (4.1), we get the following equation in $Q$:

$$C_4 Q^4 + C_3 Q^3 + C_2 Q^2 + C_1 Q + C_0 = 0,$$

(4.4)
where
\[ C_4 = \theta^2(X_2 - X_3)(X_5 + X_6), \]
\[ C_5 = \mu_h \theta(X_2 - X_3)[X_5(1 + \theta) + X_6\{r + \theta(1 - r)\}] + \theta \mu_h (X_5 + X_6)[X_2(1 + \theta) - X_3\{r + \theta(1 - r)\}] - X_1 X_4 \theta^2, \]
\[ C_2 = \theta X_5 \mu_h^2(X_2 - X_3) + \mu_h^2[X_2(1 + \theta) - X_3\{r + \theta(1 - r)\}][X_5(1 + \theta) + X_6\{r + \theta(1 - r)\}] + X_2 \mu_h^2(X_5 + X_6) - X_1 X_4 \theta \mu_h \{r + \theta(1 - r)\} - X_1 X_4 \theta \mu_h (1 + \theta), \]
\[ C_1 = X_5 \mu_h^2[X_2(1 + \theta) - X_3\{r + \theta(1 - r)\}] + X_2 \mu_h^2[X_5(1 + \theta) + X_6\{r + \theta(1 - r)\}] - X_1 X_4 \mu_h^2(1 + \theta)\{r + \theta(1 - r)\} - X_1 X_4 \mu_h^2. \]
\[ C_0 = X_2 X_5 \mu_h - X_1 X_4 \mu_h^3\{r + \theta(1 - r)\} = \pi_h^2 \mu_h^2 \mu_v (1 - R_0^2) \]

with
\[
X_1 = \frac{\pi_h \gamma_h}{\mu_h + \gamma_h} \left[ \frac{1 - \rho}{\mu_h + \eta + q_2 + p_2} + \frac{\lambda \rho}{\mu_h + q_1 + p_1} \right], \quad X_2 = \frac{\pi_h}{\mu_h}, \\
X_3 = \frac{\delta \pi_h \gamma_h}{\mu_h (\mu_h + \gamma_h)(\mu_h + \delta + q_3)} \left[ \frac{p_1 \rho}{\mu_h + q_1 + p_1} + \frac{(1 - \rho)(q_2 + p_2)}{\mu_h + \eta + q_2 + p_2} \right], \\
X_4 = \frac{\beta^2 \alpha_v \pi_v \mu_v}{\mu_v (\mu_v + \gamma_v)} X_5 = \mu_v X_2, \quad X_6 = \beta \alpha_h X_1 - \mu_v X_3. 
\]

By employing the Descartes’ rule of signs on the equation given in (4.4), we list the various possibilities for the positive roots of this equation in Table 3 [44].

### 4.1.1. Global stability of the endemic equilibrium

Using the fact that \( N_h = S_{h1} + S_{h2} + E_h + A_h + I_h + P_h + R_h \), we have the following system:

\[
\begin{align*}
\frac{dS_h}{dt} &= \pi_v - \beta \alpha_h S_v \left( \frac{I_h + \lambda A_h}{N_h} \right) - \mu_v S_v, \\
\frac{dE_h}{dt} &= \beta \alpha_h S_v \left( \frac{I_h + \lambda A_h}{N_h} \right) - (\gamma_v + \mu_v) E_v, \\
\frac{dI_h}{dt} &= \gamma_v E_v - \mu_v I_v, \\
\frac{dN_h}{dt} &= \pi_h - \mu_h N_h - \delta P_h, \\
\frac{dS_{h2}}{dt} &= (1 - r) \pi_h - \beta \theta \alpha_v I_v \left( \frac{S_{h2}}{N_h} \right) - \mu_h S_{h2}, \\
\frac{dE_{h2}}{dt} &= \beta \alpha_v I_v \left( \frac{(N_h - S_{h2} - E_h - A_h - I_h - P_h - R_h) + \theta S_{h2}}{N_h} \right) - (\gamma_h + \mu_h) E_h, \\
\frac{dA_h}{dt} &= \rho \gamma_h E_h - (\mu_h + q_1 + p_1) A_h, \\
\frac{dI_h}{dt} &= (1 - \rho) \gamma_h E_h - (\mu_h + \eta + q_2 + p_2) I_h, \\
\frac{dP_h}{dt} &= p_1 A_h + (\eta + p_2) I_h - (q_3 + \mu_h + \delta) P_h, \\
\frac{dR_h}{dt} &= q_1 A_h + q_2 I_h + q_3 P_h - \mu_h R_h.
\end{align*}
\]
Table 3: Number of possible positive real roots of Eq. (4.4) for $R_0 < 1$ and $R_0 > 1$.

| Cases | $C_4$ | $C_4$ | $C_2$ | $C_1$ | $C_0$ | $R_0 < 1$ | $R_0 > 1$ | No. of sign changes | No. of possible positive real roots |
|-------|-------|-------|-------|-------|-------|-----------|-----------|---------------------|---------------------------------|
| 1.    | +     | +     | +     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 0                   | 0                               |
|       | +     | +     | +     | -     |       | 1         | 1         | 1                   | 1                               |
| 2.    | +     | -     | -     | -     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | +     | -     | -     | -     |       | 1         | 1         | 1                   | 1                               |
| 3.    | +     | -     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | +     | +     | -     | -     |       | 1         | 1         | 1                   | 1                               |
| 4.    | +     | -     | +     | -     | +     | $R_0 < 1$ | $R_0 > 1$ | 4                   | 0,2,4                           |
|       | +     | +     | -     | +     | -     | 3         | 1,3       | 1                   | 1                               |
| 5.    | +     | -     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | +     | -     | -     | -     |       | 3         | 1,3       | 1                   | 1                               |
| 6.    | +     | +     | +     | -     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | +     | +     | -     | -     |       | 1         | 1         | 1                   | 1                               |
| 7.    | +     | +     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 3                   | 1,3                             |
|       | +     | -     | +     | +     |       | 2         | 1         | 1                   | 1                               |
| 8.    | +     | -     | +     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 3                   | 1,3                             |
|       | +     | +     | +     | -     |       | 1         | 1         | 1                   | 1                               |
| 9.    | -     | +     | +     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | -     | +     | +     | -     |       | 2         | 1         | 1                   | 1                               |
| 10.   | -     | -     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 1                   | 1                               |
|       | -     | -     | -     | -     |       | 1         | 1         | 1                   | 1                               |
| 11.   | -     | -     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 0                   | 0                               |
|       | -     | +     | -     | -     |       | 2         | 0,2       | 1                   | 1                               |
| 12.   | -     | -     | +     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 3                   | 1,3                             |
|       | -     | -     | +     | -     | +     | 2         | 0,2       | 1                   | 1                               |
| 13.   | -     | -     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
|       | -     | +     | -     | +     | -     | 3         | 1,3       | 1                   | 1                               |
| 14.   | -     | +     | +     | -     | +     | $R_0 < 1$ | $R_0 > 1$ | 4                   | 0,2,4                           |
|       | -     | +     | -     | +     | -     | 1         | 1         | 1                   | 1                               |
| 15.   | -     | +     | -     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 4                   | 0,2,4                           |
|       | -     | +     | -     | -     |       | 2         | 0,2       | 1                   | 1                               |
| 16.   | -     | -     | +     | +     | +     | $R_0 < 1$ | $R_0 > 1$ | 2                   | 0,2                             |
Since system (4.5) is equivalent to the system (2.1), we study the global asymptotic stability of the endemic equilibrium $E^*(S^*_v, E^*_v, I^*_v, \beta^*_v, N^*_h, S^*_h, E^*_h, I^*_h, P^*_h, R^*_h)$ of the system (4.5).

Regarding global asymptotic stability of the equilibrium $E^*$, we have the following theorem.

**Theorem 4.1.** The equilibrium $E^*$ is globally asymptotically stable inside the region of attraction $\Omega$, provided the following inequalities hold:

$$
\max \left\{ \frac{15}{2\mu_h} \left[ \frac{\beta_\alpha_v \left( \pi_h - \mu_h S^*_h - E^*_h - I^*_h + P^*_h + \frac{R^*_h}{\mu_h + \delta} \right)}{\pi_h / (\mu_h + \delta)} \right]^2, \frac{9}{2\mu_v} \left[ \frac{\beta_\alpha_v \left( \pi_h / (\mu_h + \delta) + \theta \pi_h / (\mu_v N^*_h) \right)}{\pi_h / (\mu_h + \delta)} \right]^2, \frac{9 N^*_h}{2(\beta_\alpha_v I^*_v + \mu_h N^*_h)} \left[ \frac{\beta_\alpha_v I^*_v / \mu_v N^*_h}{\pi_h / (\mu_h + \delta)} \right]^2 \right\} < [\gamma_h + \mu_h],
$$

$$
\max \left\{ \frac{5}{\mu_h} \left[ \frac{\beta_\alpha_v \left( 1 + \lambda \right) / (\mu_h + \delta)}{\mu_v / \mu_h N^*_h} \right]^2, \frac{5}{\mu_h + \eta + q_2 + p_2} \left[ \frac{\beta_\alpha_v \pi_v}{\mu_v N^*_h} \right]^2, \frac{5}{\mu_h + \eta + q_2 + p_2} \left[ \frac{\beta_\alpha_v \pi_v}{\mu_v N^*_h} \right]^2 \right\} < [\gamma_v + \mu_v],
$$

$$
\max \left\{ \frac{5}{\mu_h} \left[ \frac{\beta_\alpha_v \left( 1 + \lambda \right) / (\mu_h + \delta)}{\mu_v / \mu_h N^*_h} \right]^2, \frac{5}{\mu_h + \eta + q_2 + p_2} \left[ \frac{\beta_\alpha_v \pi_v}{\mu_v N^*_h} \right]^2, \frac{5}{\mu_h + \eta + q_2 + p_2} \left[ \frac{\beta_\alpha_v \pi_v}{\mu_v N^*_h} \right]^2 \right\} < \frac{4}{\gamma_v + \mu_v} \left[ \frac{\beta_\alpha_v \left( I^*_v + \lambda A^*_h \right)}{N^*_h} \right]^2,
$$

$$
\max \left\{ \frac{5 q_1^2}{\mu_h + q_1 + p_1}, \frac{5 q_2^2}{\mu_h + \eta + q_2 + p_2}, \frac{5 q_3^2}{\mu_h + \delta + q_3}, \frac{5 q_4^2}{\mu_h + \delta + q_4}, \frac{15 N^*_h}{4(\beta_\alpha_v I^*_v + \mu_h N^*_h)} \left[ \frac{\beta_\alpha_v \pi_v / (\mu_v N^*_h)}{\mu_h + \eta + q_2 + p_2} \right]^2 \right\} < \mu_h,
$$

$$
\max \left\{ \frac{[\beta_\pi_\alpha v / (\mu_h N^*_h)]^2}{\mu_v N^*_h} \right\} < \frac{4}{9} \frac{\mu_v + \beta_\alpha_v I^*_v}{N^*_h},
$$

$$
\max \left\{ \frac{(\eta + p_2)^2}{\mu_h + \eta + q_2 + p_2}, \frac{p_1^2}{\mu_h + \eta + q_2 + p_2}, \frac{p_1^2}{\mu_h + \eta + q_2 + p_2} \right\} < \frac{4(\mu_h + \delta + q_3)}{25}.
$$

For proof of this theorem, see Appendix C.

**Remark 4.1.** Conditions of Theorem 4.1 are only sufficient for the global asymptotic stability of the equilibrium $E^*$ and prevents persistent oscillations of the system solutions.

To verify above theorem numerically, we choose the following set of hypothetical parameter values in the system (2.1)

$$
\pi_v = 8, \ beta = 2, \ mu_v = 0.3, \ gamma = 0.795, \ pi_h = 0.15, \ mu_h = 0.154, \ gamma_h = 0.3, \ q_1 = 0.4, \ delta = 0.5, \ alpha_h = 0.75, \ lambda = 0.5, \ r = 0.55, \ alpha_v = 0.05, \ theta = 0.85, \ rho = 0.25, \ q_2 = 0.355, \ q_3 = 0.5972, \ eta = 1.474 \ p_1 = 0.01, \ p_2 = 0.02.
$$
The components of the equilibrium $E^*$ are found to be

$$S^*_v = 21.3803, \quad E^*_v = 1.4483, \quad I^*_v = 3.8380, \quad S^*_{h1} = 0.1385, \quad S^*_{h2} = 0.1275,$$

$$E^*_h = 0.2402, \quad A^*_h = 0.0319, \quad I^*_h = 0.0270, \quad P^*_h = 0.0325, \quad R^*_h = 0.2711.$$

For above set of parameter values, the conditions for the global asymptotical stability of the equilibrium $E^*$ are satisfied. We show the global stability of the endemic equilibrium $E^*$ inside the region $\Omega$ in $S_v - E_v - I_v$ and $E_h - A_h - I_h$ spaces, Fig. 2. It is evident from the figure that all the solution trajectories that originate inside the region of attraction $\Omega$ approach the point $(S^*_v, E^*_v, I^*_v)$ and $(E^*_h, A^*_h, I^*_h)$, as shown in Fig. 2a and Fig. 2b, respectively. Thus, the numerical results also confirm that the endemic equilibrium $E^*$ is globally asymptotically stable in the $S_v - E_v - I_v$ and $E_h - A_h - I_h$ spaces. Using this approach, we can show the global asymptotic stability of the endemic equilibrium $E^*$ in other spaces.

5. Sensitivity analysis

To see the effect of some controllable parameters, $\beta, \mu_v, \eta, p_1$ and $p_2$, of the system (2.1) on the value of basic reproduction number, $R_0$, we calculate the normalized forward sensitivity indices of $R_0$ to these parameters. We evaluate the sensitivity indices for $\beta = 42.885$, $\eta = 0.0119$, $p_1 = 0.3$ and $p_2 = 0.2$, and taking rest of the parameter values from Table 2. The normalized forward sensitivity index for a variable $w$, which depends differentiably on a parameter $\alpha$, is defined as

$$X^\alpha_w = \frac{\partial w}{\partial \alpha} \times \frac{\alpha}{w}.$$

The sensitivity indices of $R_0$ with respect to the parameters $\beta, \mu_v, \eta, p_1$ and $p_2$ are found to be

$$X^\beta_{R_0} = 1, \quad X^{\mu_v}_{R_0} = -1, \quad X^\eta_{R_0} = -0.1476, \quad X^{p_1}_{R_0} = -0.0255, \quad X^{p_2}_{R_0} = -0.1990.$$

The fact that $X^\beta_{R_0} = 1$ means that 1% increase in $\beta$, keeping other parameters fixed, will produce 1% increase in $R_0$. When the parameters $\mu_v, \eta, p_1$ and $p_2$ increase by 1% while keeping other parameters
constant, the value of $R_0$ decreases by 1%, 0.1476%, 0.0255% and 0.1990%, respectively. Overall a lower value of $R_0$ is preferable because it increases the possibility of disease eradication in the region. Therefore, above all prevention practices must focus on a decrease in the parameter $\beta$, while an increase in the parameters $\mu_v$, $\eta$, $p_1$ and $p_2$ should instead be favored.

Further, to check how the total infective populations $(A_h + I_h + P_h)$ are affected with variations in average biting rate of mosquito, death rate of mosquito, rate of hospitalization and/or notification of symptomatic individuals, and ACF of asymptomatic and symptomatic individuals, we perform semi-relative sensitivity analysis of the system (2.1) [45]. We plot the semi-relative sensitivity solutions of the total infective populations $(A_h + I_h + P_h)$ with respect to $\beta$, $\mu_v$, $\eta$, $p_1$ and $p_2$ in Fig. 3. From the figure, we can see that doubling of these parameters exhibit their largest influences early in the simulation and a large expected variation in the total infected populations is observed. It is apparent from the figure that the doubling of $\beta$ and $\mu_v$ will yield sudden increase and decrease of total infected populations, respectively around $t = 10$ years. Sudden increase in the total infected population on doubling of $\beta$ is due to a large number of initial susceptible population. As time progresses, the susceptible population decreases and on natural recovery, the infective decreases. Similarly, the infective decreases by a large number by doubling $\mu_v$ on its initial phase but with increase in time, the infective first increases and then again decreases. On the other hand, $\eta$ exhibits maximum reduction in total infected population around $t = 10$ years and no further reduction is observed. Such decrease in total infected population is due to insufficient mosquito control and personal protection. Increase in the parameters due to active case finding reduce the prevalence of the disease. Note here that the parameters $\beta$, $\mu_v$, and $p_2$ have larger effects in comparison to the other two parameters on the total infective population. Therefore, they play crucial roles for the control of the disease. Moreover, the impacts of $\eta$ and $p_1$ are also important.
6. Data and model calibration

India experienced high levels of dengue cases in recent years. In 2017, a provisional total of 1,88,401 cases has been reported to NVBDCP [39]. We use annual reported cases of dengue fever in eight states of India to calibrate the model (2.1) in the absence of ACF parameters, $p_1$ and $p_2$. The reason behind dropping the ACF parameters is that currently ACF is not employed in India for dengue control. For our study, we choose Kerala, Delhi, Gujarat, West Bengal, Andhra Pradesh, Rajasthan, Maharashtra and Karnataka, dengue endemic states of India.

We estimate the unknown parameters $\hat{\theta} = (\beta, \eta)$ using the annual new dengue cases from 2007 to 2017 [38, 39]. All the fixed parameters are taken from Table 2. Let $P(t, \hat{\theta})$ denote the number of new hospitalized and/or notified dengue cases from model (2.1) at the $t^{th}$ year, then $P(t, \hat{\theta})$ has the form

$$P(t, \hat{\theta}) = \int_{t-1}^{t} [\eta I_h] \, dt,$$

and if $C(0)$ is the number of new hospitalized and/or notified dengue cases at the first time point of the data, then $P(0) = C(0)$. We have $R$ independent observations from data, representing the number of new hospitalized and/or notified dengue cases in the $i^{th}$ year, where $i = 1, \cdots, R$. Let $\epsilon$ be the error of fit, which follows the Gaussian distribution having an unknown variance $\sigma^2$

$$Y_i = P(t_i, \hat{\theta}) + \epsilon, \epsilon \sim N(0, I\sigma^2).$$

We draw initial samples of $\hat{\theta}$ using the LHS technique, then obtain an estimate of each sample by finding local minima of $SS(\hat{\theta})$ using Nonlinear Least-Square techniques. The lowest value of $SS(\hat{\theta})$ is found and the corresponding $\hat{\theta}$ is chosen as the initial guess in the MCMC Toolbox [46]. Further, the convergence of chain is also confirmed using the Gewekes Z-scores, Table 4. From the table, we see that the biting rates of mosquitoes, $\beta$, are higher in Andhra Pradesh, Rajasthan, Gujarat and Maharashtra. High rates of biting rate in these states may be due to large number of mosquitoes populations and/or lack of personal protection. Moreover, the rate of hospitalization and/or notification of symptomatic humans, $\eta$, are estimated to be lower for these four states. These observations indicate that people in these four states may have less awareness about the disease.

7. Impact of ACF on dengue control

Active case finding for dengue patients is the systematic identification of people with suspected dengue, in a predetermined target area by using tests (such as SD Bioline Dengue Duo Rapid Test Kit) at a regular basis. The positive ones should be hospitalized immediately for treatment or the person should be kept in a mosquito-free environment to avoid secondary infection. However, the results from sensitivity analysis suggest that $p_2$ is more effective than $p_1$ in terms of case reduction. Now we quantify the impacts of these two parameters on the percentage reduction of dengue cases in the eight states. Using the estimated parameters (see Table 4) for each state we predict total dengue cases in the years 2018–2050. The base cases were determined by simulating the model without ACF parameters. For different values of $p_1$ and $p_2$, the case reduction in total dengue cases is depicted in Fig. 6.

All of the eight states of India shows similar patterns in case reduction by the ACF intervention. Note that the scales of averted cases is different in Fig. 6(a) and Fig. 6(b). The reason behind this is that the asymptomatic individuals are less infectious as compared to symptomatic humans. Maximum
Table 4: Estimated parameters of the system \((2.1)\) and their mean values given in 95% CI for different states of India

| States          | Parameter | Mean value | 95% Confidence interval     | Geweke’s Z-score |
|-----------------|-----------|------------|----------------------------|-----------------|
| Kerala          | \(\beta\) | 53.347     | 24.516–85.620              | 0.9029          |
|                 | \(\eta\)  | 0.0195     | 0.0018–0.1459              | 0.8079          |
| Delhi           | \(\beta\) | 42.885     | 26.2043–65.8082            | 0.8681          |
|                 | \(\eta\)  | 0.0143     | 0.0025–0.0579              | 0.8782          |
| Gujarat         | \(\beta\) | 62.224     | 46.8378–80.5926            | 0.9685          |
|                 | \(\eta\)  | 0.0042     | 0.0013–0.0112              | 0.8502          |
| West Bengal     | \(\beta\) | 47.177     | 17.4763–82.1461            | 0.8739          |
|                 | \(\eta\)  | 0.029      | 0.0014–0.1780              | 0.6305          |
| Andhra Pradesh  | \(\beta\) | 67.393     | 50.8408–85.4559            | 0.9769          |
|                 | \(\eta\)  | 0.0025     | 0.0009–0.0065              | 0.7813          |
| Rajasthan       | \(\beta\) | 62.929     | 39.723–87.823              | 0.8994          |
|                 | \(\eta\)  | 0.0043     | 0.0008–0.0176              | 0.741           |
| Maharashtra     | \(\beta\) | 60.531     | 33.4334–83.6098            | 0.9257          |
|                 | \(\eta\)  | 0.0054     | 0.0011–0.0245              | 0.7928          |
| Karnataka       | \(\beta\) | 43.572     | 19.0592–74.3453            | 0.9694          |
|                 | \(\eta\)  | 0.0126     | 0.0008–0.0645              | 0.8002          |

Employment of ACF of asymptomatic individuals will cause 0.44%, 0.30%, 0.30%, 0.48%, 0.28%, 0.37%, 0.39% and 0.39% increase in total averted cases in Kerala, Delhi, Gujarat, West Bengal, Andhra Pradesh, Rajasthan, Maharashtra and Karnataka, respectively. On the other hand maximum employ-
Figure 5: Plots of the output of the fitted model (2.1) and the observed cumulative dengue data for (a) Andhra Pradesh, (b) Rajasthan, (c) Maharashtra and (d) Karnataka. Cumulative cases (filled blue circle) from the data, and model simulated data (thick green curve) are plotted with the parameter estimates using parameter values of Table 2.

8. Conclusion and discussion

In this article, we formulated a compartmental ODE model for dengue. The model included class of hospitalized and/or notified humans who cannot transmit dengue as they are kept in a mosquito free environment. We showed positivity and boundedness of the solutions of the system (2.1). System (2.1) has a unique disease-free equilibrium which is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. We found that the parameters $\eta$, $\mu_v$, $p_1$ and $p_2$ have negative effects on $R_0$ while the parameter $\beta$ have positive effect (see Section 5). From the normalized forward sensitive indices of $R_0$ and the semi-sensitivity solutions of total infective populations, we observed that $p_2$ is more effective than $p_1$ in reducing the disease burden. Therefore, the health care organizations should pay more attention towards the active case finding of symptomatic individuals in comparison to that of asymptomatic.

System (2.1) is calibrated using yearly data of dengue from eight different states of India for the years 2007–2017. Model fitting with yearly new dengue cases is depicted in Figs. 4 and 5, and the 95% confidence intervals of the estimated parameters are given in Table 4. The estimated values of biting
rate of mosquitoes and rate of hospitalization and/or notifications show that Andhra Pradesh, Rajasthan, Gujarat and Maharashtra are at higher risks of future outbreaks. Moreover, using these parameters, we computed the number of cases averted by employing ACF in eight different states of India. It is observed that all of the eight states show similar trends of case reduction by ACF. From Fig. 6, one can easily note that ACF of symptomatic individuals will have a significant effect on dengue case reduction. On the other hand, ACF of asymptomatic humans will avert comparatively less number of dengue cases. However, it is well established that most of the dengue cases are asymptomatic. Therefore, asymptomatic humans play an important role in the persistence of dengue in the community. Complete eradication of the disease will be difficult unless we control the asymptomatic individuals. This indicates that ACF of asymptomatic individuals is not negligible in the long run.

Currently, ACF has been used as an effective control strategy against tuberculosis (TB) in India [32, 47]. Around 20 million people were tested and a large number of persons were detected positive in the year 2013-2014 [48]. The Revised National TB Control Programme (RNTCP) has decided to
implement ACF for TB in 552 districts of India among high prevalence area from 2017 onwards as part of its latest national strategic plan [47]. Recent studies showed that implementation of ACF in India can eliminate TB [47, 48]. Results of our study shows similar effects of ACF on dengue control in India. The healthcare agencies should focus on the areas with most dengue cases and employ ACF in order to reduce the raising number of dengue cases in the country. In addition, quite a huge number of missing cases reside in endemic areas of India [49, 50]. ACF will definitely help to fill up the gap of missing cases. Healthcare agencies should identify high-risk target areas and provide proper resources to run the ACF programme smoothly. Due to the twofold benefits, we recommend that along with existing control measures (personal protection and mosquitoes control), the healthcare organizations must focus on ACF, which plays a plausible role in reducing the number of dengue cases to a low endemic equilibrium level in the endemic states of India.

In future research, we may add host heterogeneity to our transmission model in order to better understand the impact of the diffusion of humans [51]. The parameters such as biting rate depends on climatic factors [52], therefore adding seasonal effects to our model will make it more realistic. Moreover, ACF strategy can be compared with recent mosquito control strategies (Ovitrap [53], virus suppressing Wolbachia infection [54] and sterile insect technique [55]) to understand the potential of these control interventions on the disease eradication.

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System (2.1) can be rewritten as

\[
\frac{dX}{dt} = CX + D,
\]
Then $0 \leq \text{state in } R = [X, \text{attracting set.}]$

$R$ positively invariant in $Z$ as $t \geq 0$.

Therefore, all feasible solutions of the system (2.1) enter the region $\Omega$ implying that the region is an attracting set.

The vector $D = [\pi, 0, 0, r\pi, (1 - r)\pi, 0, 0, 0, 0]^T$ is positive. Note that all the off-diagonal entries of $C(X)$ are nonnegative. Therefore, the matrix $C(X)$ is Metzler for all $X \in R^+$. Thus, system (2.1) is positively invariant in $R^+$. Hence, all trajectories of the system (2.1) which originate from an initial state in $R^+$ confine therein forever.

Summing up the first three equations of system (2.1), we get

$$\frac{dN_v}{dt} = \pi_v - \mu_v N_v.$$  

Using a standard comparison theorem [57], we have $0 \leq N_v(t) \leq \frac{\pi_v}{\mu_v} + \left( N_v(0) - \frac{\pi_v}{\mu_v} \right) e^{-\frac{\mu_v}{\mu_v} t}$. Thus, as $t \to \infty$, $0 \leq N_v(t) \leq \frac{\pi_v}{\mu_v}$, we have for any $t > 0$, $0 \leq N_v(t) \leq Z_1$, where $Z_1 = \max \left\{ \frac{\pi_v}{\mu_v}, N_v(0) \right\}$.

Assume that $Z_2 = \max \left\{ \frac{\pi_h}{\mu_h} S_{h1}(0) \right\}$. Then $0 \leq S_{h1} \leq Z_2$. Similarly, let $Z_3 = \max \left\{ \frac{(1 - r)\pi_h}{\mu_h}, S_{h2}(0) \right\}$.

Then $0 \leq S_{h2} \leq Z_3$.

By adding the last seven equations of the system (2.1), we get

$$\frac{dN_h}{dt} = \pi_h - \mu_h N_h - \delta P_h \leq \pi_h - \mu_h N_h.$$  

Assume that $Z_4 = \max \left\{ \frac{\pi_h}{\mu_h}, N_h(0) \right\}$. Then $N_h \leq Z_4$. Also, $\frac{dN_h}{dt} \geq \pi_h - (\mu_h + \delta) N_h$. Assume that $Z_5 = \min \left\{ \frac{\pi_h}{\mu_h + \delta}, N_h(0) \right\}$. Then $N_h \geq Z_5$. Thus, we have $Z_5 \leq N_h \leq Z_4$.

Therefore, all feasible solutions of the system (2.1) enter the region $\Omega$ implying that the region is an attracting set.
Appendix B

Jacobian of system (2.1) at the equilibrium $E_0$ is

$$J_{E_0} = \begin{bmatrix}
-\mu_v & 0 & 0 & 0 & 0 & 0 & -\beta_{bh} \lambda \pi \mu_h \\
0 & -(\gamma_v + \mu_v) & 0 & 0 & 0 & -\beta_{bh} \lambda \pi \mu_h \\
0 & \gamma_v & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & -\mu_h \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix}.$$  

Five eigenvalues of the matrix $J_{E_0}$ are $-\mu_v$, $-\mu_h$ (of multiplicity 3) and $-(\mu_h + \delta + q_3)$, and other five are given by the roots of the equation

$$\rho^5 + A_1 \rho^4 + A_2 \rho^3 + A_3 \rho^2 + A_4 \rho + A_5 = 0,$$

where

$$A_1 = 2\mu_v + 3\mu_h + \eta + \gamma_v + \gamma_h + q_1 + q_2 + p_1 + p_2,$$

$$A_2 = (\mu_h + \eta + q_2 + p_2)(2\mu_v + 2\mu_h + \gamma_v + \gamma_h + q_1 + p_1) + (\mu_h + q_1 + p_1)(2\mu_v + \mu_h + \gamma_v + \gamma_h) + \mu_v(\gamma_v + \mu_v) + (\gamma_h + \mu_h)(\gamma_v + 2\mu_v),$$

$$A_3 = (\mu_h + \eta + q_2 + p_2)(\mu_h + q_1 + p_1)(2\mu_v + \mu_h + \gamma_v + \gamma_h + \mu_v(\gamma_v + \mu_v) + (\gamma_h + \mu_h)(\gamma_v + 2\mu_v)), $$

$$A_4 = (\mu_h + \eta + q_2 + p_2)(\mu_h + q_1 + p_1)\left\{\mu_v(\gamma_v + \mu_v) + (\gamma_h + \mu_h)(\gamma_v + 2\mu_v) \right\} + \frac{\beta^2 \alpha v \alpha h \gamma v \pi h \mu h (r + \theta(1 - r))}{\mu h \pi h} \left[\frac{(\mu_h + \eta + q_2 + p_2) A \rho}{\mu_h + q_1 + p_1} + (\mu_h + q_1 + p_1) (1 - \rho) \right]$$

$$+ \mu_v(\mu_h + \gamma_h)(\mu_v + \gamma_v)(2\mu_h + \eta + q_1 + q_2 + p_1 + p_2)(1 - R_0^2),$$

$$A_5 = \mu_v(\gamma_v + \mu_v)(\gamma_h + \mu_h)(\mu_h + q_1 + p_1)\mu_h + \eta + q_2 + p_2)(1 - R_0^2).$$

Clearly, all roots of equation (8.1) are either negative or have negative real parts if $R_0 < 1$. Thus, the disease-free equilibrium $E_0$ is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Appendix C

Consider the following positive definite function

$$V = \frac{1}{2}[(S_v - S_v^*)^2 + (E_v - E_v^*)^2 + (I_v - I_v^*)^2 + (N_h - N_h^*)^2 + (S_{h2} - S_{h2}^*)^2]$$

$$+ (E_h - E_h^*)^2 + (A_h - A_h^*)^2 + (I_h - I_h^*)^2 + (P_h - P_h^*)^2 + (R_h - R_h^*)^2].$$

Differentiating equation (8.2) with respect to time ‘t’ along the solution trajectories of system (4.5)
and rearranging the terms, we get

\[
\frac{dV}{dt} = - \left[ \mu_v + \beta \alpha_h \left( \frac{I_v + \lambda A_v^*}{N_h^*} \right) \right] (S_v - S_v^*)^2 - [\gamma_v + \mu_v](E_v - E_v^*)^2 - [\mu_v](I_v - I_v^*)^2 \\
- \mu_h(N_h - N_h^*)^2 - \left[ \theta \beta \alpha_v I_v^* \right] + \mu_h \left( S_{h2} - S_{h2}^* \right)^2 - \left[ \frac{\beta \alpha_v I_v}{N_h^*} + \gamma_h + \mu_h \right] (E_h - E_h^*)^2 \\
- \left[ \mu_h + q_1 \right] (A_h - A_h^*)^2 - \left[ \mu_h + \eta + q_2 + p_1 \right] (I_h - I_h^*)^2 - \left[ q_3 + \mu_h + \delta \right] (P_h - P_h^*)^2 - \left[ \mu_h \right] (R_h - R_h^*)^2 \\
- \frac{\beta \alpha_h S_v (I_h + \lambda A_h)}{N_h N_h^*} (S_v - S_v^*) (N_h - N_h^*) - \frac{\beta \alpha_h S_v (I_h + \lambda A_h)}{N_h N_h^*} (S_v - S_v^*) (I_h - I_h^*) - \frac{\beta \lambda \alpha_h}{N^*} (S_v - S_v^*) (A_h - A_h^*) \\
+ \frac{\beta \alpha_h (I_h + \lambda A_h)}{N_h} (S_v - S_v^*) (E_v - E_v^*) + \frac{\beta \alpha_h S_v (I_h + \lambda A_h)}{N_h N_h^*} (E_v - E_v^*) (N_h - N_h^*) \\
+ \frac{\beta \alpha_h S_v}{N_h} (E_v - E_v^*) (I_h - I_h^*) + \frac{\beta \lambda \alpha_h S_v}{N^*} (E_v - E_v^*) (A_h - A_h^*) + [\gamma_v] (E_v - E_v^*) (I_v - I_v^*) \\
- \delta (N_h - N_h^*) (P_h - P_h^*) - \frac{\beta \alpha_v I_v S_h^2}{N_h N_h^*} (N_h - N_h^*) (S_{h2} - S_{h2}^*) - \frac{\beta \alpha_v S_h^2}{N_h^*} (I_v - I_v^*) (S_{h2} - S_{h2}^*) \\
+ \frac{\beta \alpha_v}{N_h N_h^*} \left[ I_v^* (S_{h2} + E_h^* + A_h^* + P_h^* + R_h^*) + \theta S_h^2 I_v \right] (N_h - N_h^*) (E_h - E_h^*) \\
+ \beta \alpha_v \left[ \frac{N_h - S_h^* - E_h^* - A_h^* - P_h^* - R_h^* + \theta S_h^2}{N_h} \right] (I_v - I_v^*) (E_h - E_h^*) \\
+ \beta \alpha_v \left[ \frac{\theta I_v^*}{N_h} - \frac{I_v}{N_h} \right] (S_{h2} - S_{h2}^*) (E_h - E_h^*) - \frac{\beta \alpha_v I_v}{N_h} (E_h - E_h^*) (P_h - P_h^*) \\
- \frac{\beta \alpha_v I_v}{N_h} (E_h - E_h^*) (R_h - R_h^*) + \left[ \rho \gamma_h - \frac{\beta \alpha_v I_v}{N_h} \right] (E_h - E_h^*) (A_h - A_h^*) \\
+ \left[ 1 - \rho \gamma_h \right] \frac{\beta \alpha_v I_v}{N_h} (E_h - E_h^*) (I_h - I_h^*) + [q_1] (A_h - A_h^*) (P_h - P_h^*) + \left[ \eta + p_2 \right] (I_h - I_h^*) (P_h - P_h^*) \\
+ [q_3] (A_h - A_h^*) (R_h - R_h^*) + [q_2] (I_h - I_h^*) (R_h - R_h^*) + [q_3] (P_h - P_h^*) (R_h - R_h^*) \right].
\]

Inside the region of attraction $\Omega$, $\frac{dV}{dt}$ can be made negative definite provided the inequalities (4.6)–(4.11) hold.