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Mathematical Model of HIV and Cholera Co-Infection in the Presence of Treatment

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Abstract : In the current study, a deterministic mathematical model of HIV and Cholera co-infection is developed to analyze the impact of treatments in the presence of diseases in the population. The model consists of nine classes of the human population and one class of bacteria population. The formulated model is mathematically well-posed and biologically meaningful. The reproduction number is employed to analyze the extinction or spreading of the disease in the population. it is observed that, cholera has a positive impact on HIV patients and HIV also has a positive impact on the cholera patients. The separate analysis of each infection model and co-infection model are presented. Further, the stability analysis of equilibrium points is included. Finally, numerical simulations are performed using Matlab software. The result of numerical simulations shows that early treatment is very powerful for clearing or controlling cholera within specified period of time and supports HIV/AIDS patients to live more years.

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1. Introduction

In 1981 a disease known as acquired immunodeficiency syndrome shortened as AIDS was discovered. AIDS is caused by infection known as human immunodeficiency virus shortened as HIV. Since then, it has been a cause of death for millions of people all over the world. AIDS patients are very weaken groups and unable to resist other diseases [10, 11, 1, 2, 4].

Nowadays, HIV/AIDS is the most threatening disease for all humans and exposes a body to be easily attacked by pathogens. HIV/AIDS disease attacks all human beings without distinguishing color and race. HIV infection drops the number of key cells called $CD4^+$T cells, in the infected human body. These $CD4^+$T-cells facilitate communication in controlling and regulating body immune system. HIV cannot be cured by any treatment, but antiretroviral therapy (ART) can reduce the number of virus cells duplicated in the body or slow the advanced stage of the virus. The transmission mode of HIV disease is through unsafe sex, blood transfusion, virus exposed. The transmission mode of HIV disease is through unsafe sex, blood transfusion, virus exposed materials, etc [10, 11]. Even though many scholars studied HIV, to control and prevent the transmission

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dynamics of the disease, still it persist in the population. Today there are millions of people living with HIV and many people are killed because of this disease. Today there are millions of people living with HIV and many are facing different challenges because of this disease [4,5].

Cholera is a contagious intestine disease that kills patients within hours if left untreated. Medical facts shows that cholera can be caused by bacterium called vibrio cholera that exists in aquatic environment. This infection results in dehydration and so far killed millions of people. Cholera was first described by a physician called Hippocrates, the most powerful and tough person in the history of medicine. Cholera infected person shows symptoms like continuous vomiting and diarrhea [6,9,8]. As log as our knowledge the previous study done on HIV and Cholera coinfections has not depicited the impact of treatments. Thus, this study is carried out to show the impact of treatments in the presence of HIV and cholera infections in the community.

Organization of the paper: In Section 2, assumptions are stated and mathematical model is formulated. In sections 3-5, well possedness of the model, stability analysis of the equilibrium points and reproduction number of cholera only, HIV only and co-infection model are presented respectively. In Section 6, numerical simulations are performed. In Section 7 discussion of sensitivity analysis is presented. In section 8, Result and Discussion are presented. Finally, the paper ends with concluding remarks in Section 9.

2. Model formulation

In this paper, a ten dimensional deterministic model is developed to analyze dynamics and impact of HIV, Cholera and HIV–Cholera infections in human population. Scholars devoted to study the impact of each disease for a long period of time. In this paper, we modified a model developed in [7] to include impact of treatment that has not studied in the base model. The current model describes the siginificant impact of treatment on both both infections in the population population. The base model has five compartments whereas the modified present model consists of ten compartment with nine classes of human population and one class of bacteria population. Each classes are described as follows: (i) Susceptible individuals. They are infection free class of human population but have a chance to be infected if exposed to bacterial environment. The size of susceptible population is denoted by $S(t)$. (ii) Cholera individuals. They are classes of human population who are infected with cholera disease. The size of cholera individuals at time t is denoted by $I_c(t)$. These individuals can be recovered from the disease at recovery rate if treated properly and on time (iii) Recovered individuals. They are individuals who get recovered from cholera infection. The size of recovered population is denoted by $R(t)$. (iv) HIV individuals. They are individuals in human population who get infected with human immunodeficiency syndrome. The size of HIV individuals is denoted by by $I_h(t)$. (v) HIV–Cholera individuals. They are individuals who get infected with both HIV and Cholera as consequence of exposure of HIV individuals to the bacterial environment. The size of HIV– Cholera individuals is denoted by $I_{hc}(t)$. (vi) Cholera recovered HIV individuals. They are HIV infected human individuals who get recovered from Cholera infection. The size of this individuals at time t is denoted by $R_h(t)$. (vii) AIDS individuals. They are human individuals who are at advanced stage of HIV. Further, individuals in this class are very weak to resist other infections or at serious or high risk to be easily attacked. The size of this individuals at time t is denoted by $A(t)$. (viii) Cholera–AIDS individuals. They are individuals who get infected with both AIDS and cholera infections. The size of these individuals at time t is denoted by $A_c(t)$. (ix) Cholera recovered AIDS individuals. They are AIDS humans who get recovered from cholera infection. The size of these individuals at time t is denoted by

$R_A(t)$. (x) Bacteria population. This is a bacteria region that can potentially affect human population provided that sufficient contact is made with the environment. The size of these individuals at time t is denoted by $B(t)$.

Moreover, the following assumptions are stated to describe HIV- Cholera model.

(i) The total size of population is assumed to be non-constant.

(ii) The total population size at time t is denoted by $N(t)$ is given by $N(t) = S(t) + I_c(t) + R(t) + I_h(t) + I_{hc}(t) + I_h(t) + R_h(t) + A(t) + A_c(t) + B(t)$

(iii) Susceptible humans are recruited to the compartment $S(t)$ at some constant rate τ.

(iv) Susceptible humans get HIV infection at a constant rate β_h.

(v) Susceptible humans get cholera infection from the environment at an ingestion rate β_c.

(vi) κ is half saturation constant of bacterium population.

(vii) $\frac{B}{\kappa+B}$ is the measure of probality of individuals with infection symptoms.

(viii) All categories of humans face the same natural mortality at a rate μ.

(ix) Cholera individuals die, because of the disease, at the rate δ_1.

(x) HIV-Cholera individuals die, because of the disease, at the rate δ_2.

(xi) AIDS individuals die, because of the disease, at the rate δ_3.

(xii) AIDS-Cholera individuals die, because of the disease, at the rate δ_4.

(xiii) Cholera recovered AIDS individuals die, because of the disease, at the rate δ_5.

(xiv) All parameters used in the dynamical system are non-negative.

(xv) Bacteria population die natural at the rate ν.

(xvi) Cholera only infected individuals release bacteria at the rate η.

(xvii) HIV individuals transfer to AIDS individuals at the rate γ.

(xviii) Recovered HIV individuals transfer to AIDS at the rate θ.

(xix) AIDS–Cholera individuals recover at the rate ϕ.

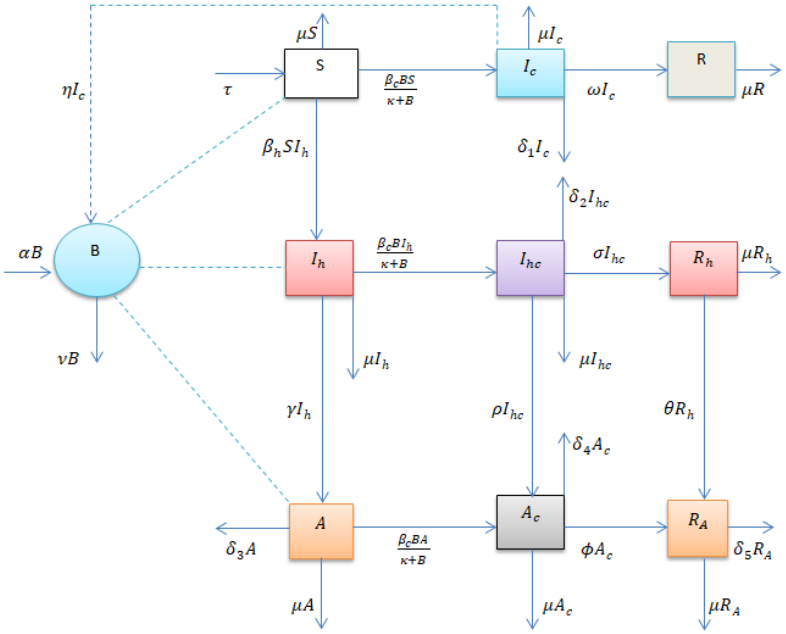

Figure 1. Flow diagram of HIV-Cholera model.

Based on the facts and assumtions on diseases the developed new model is given by

$$dS/dt = \tau - \frac{\beta_c BS}{\kappa + B} - \beta_h S I_h - \mu S \quad (1)$$

$$dI_c/dt = \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu) I_c \quad (2)$$

$$dR/dt = \omega I_c - \mu R \quad (3)$$

$$dI_h/dt = \beta_h S I_h - \frac{\beta_c B I_h}{\kappa + B} - (\gamma + \mu) I_h \quad (4)$$

$$dI_{hc}/dt = \frac{\beta_c B I_h}{\kappa + B} - (\rho + \sigma + \delta_2 + \mu) I_{hc} \quad (5)$$

$$dA/dt = \gamma I_h - \frac{\beta_c BA}{\kappa + B} - (\delta_3 + \mu) A \quad (6)$$

$$dA_c/dt = \frac{\beta_c BA}{\kappa + B} + \rho I_{hc} - (\phi + \delta_4 + \mu) A_c \quad (7)$$

$$dR_h/dt = \sigma I_{hc} - (\theta + \mu) R_h \quad (8)$$

$$dR_A/dt = \theta R_h + \phi A_c - (\delta_5 + \mu) R_A \quad (9)$$

$$dB/dt = \alpha B + \eta I_c - \nu B \quad (10)$$

The non-negative initial conditions of the model equations (1) – (10) are denoted by $S(0) \geq 0,\ I_c(0) \geq 0, R(0) \geq 0,\ I_h(0) \geq 0,\ I_{hc}(0),\ A(0) \geq 0, A_c \geq 0, R_h \geq 0,\ R_A \geq 0,\ B(0) \geq 0$. This system consists of four first order non-linear ordinary differential equations.

3. Mathematical analysis of the Cholera only model

The Cholera only model is obtained from the model (1)-(10) by setting $I_h = I_{hc} = A = sA_c = R_h = R_A = 0$. Then we get:

$$dS/dt = \tau - \frac{\beta_c BS}{\kappa + B} - \mu S \quad (11)$$

$$dI_c/dt = \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu) I_c \quad (12)$$

$$dR/dt = \omega I_c - \mu R \quad (13)$$

$$dB/dt = \alpha B + \eta I_c - \nu B \quad (14)$$

3.1 *Invariant region*

Theorem 3.1 The model (11)-(14) has a bounded solution in the region Ω for all $t > 0$.

Proof Let $x = (S,\ I_c,\ R,\ B) \in \Re_+^4$ represents a solution of a considered model (11)–(14) with the given initial conditions in the invariant region Ω. In order to analyze boundedness we categorize total population into two groups: Human population and Bacteria population. Let $N_T(t)$ represents total population size at time t such that the following is true.

$$N_T(t) = N(t) + B(t)$$

where, $N(t)$ represents the total size of human population and $B(t)$ represents the total size of bacteria population.

Now systematically and logically, we consider two regions Ω_1 and Ω_2 to handle the proof of the theorem easily. (i) let Ω_1 be invariant region that consists of three solution

variables of human population with the given initial conditions. Moreover, consider total size of human population, $N(t)$, at time t which is given by

$$N(t) = S(t) + I_c(t) + R(t)$$

Now differentiating both sides of equation of total population with respect to time t we get

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_c}{dt} + \frac{dR}{dt}$$
$$\Rightarrow \frac{dN}{dt} = \tau - \mu N - \delta_1 I_c \leq \tau - \mu N$$
$$\Rightarrow dN/dt \leq \tau - \mu N$$
$$\Rightarrow dN/(\tau - \mu N) \leq dt$$

Integrating both sides of $dN/(\tau - \mu N) \leq dt$ over $[0\ t]$ we have,

$$\int_0^t \frac{1}{\tau - \mu N} dN \leq \int_0^t dt$$
$$\Rightarrow \frac{\tau - \mu N(t)}{\tau - \mu N(0)} \geq e^{-\mu t} \quad [\text{Assuming } N(0) < \frac{\tau}{\mu}]$$
$$\Rightarrow \tau - \mu N(t) \geq \big(\tau - \mu N(0)\big)e^{-\mu t}$$
$$\Rightarrow N(t) \leq (\tau/\mu) - \big(\tau/\mu - N(0)\big)e^{-\mu t}$$

Now as $t \longrightarrow \infty$, we conclude that,

$$N(t) \leq \tau/\mu$$

Now it follows that, $0 \leq N(t) \leq \tau/\mu$. Thus, all solution variables of human population are bounded in Ω_1. That is,

$$\Omega_1 = \left\{\big((S,\quad I_c,\quad R) \in \Re_+^3\big) \in \Re_+^3 : 0 \leq N(t) \leq \tau/\mu\right\}$$

Similarly, let $B(t)$ represents population size of bacterial population, with bounded initial condition. Now (4) gives,

$$dB/dt = \alpha B + \eta I_c - \nu B \leq (\alpha - \nu)B + \frac{\eta\tau}{\mu}$$
$$\Rightarrow \frac{dB}{(\alpha - \nu)B + \eta\tau/\mu} \leq dt$$

Integrating both sides of $\frac{dB}{(\alpha-\nu)B+\eta\tau/\mu} \leq dt$ over [0 t] and assuming $0 < \alpha < \nu$, we get,

$$B(t) = \eta\tau/\mu(\nu - \alpha) - (B_0 + \eta\tau/\mu(\nu - \alpha))e^{-(\nu-\alpha)t}$$

Now as $t \longrightarrow \infty$,it follows that,

$$B(t) \leq \eta\tau/\mu(\nu - \alpha)$$

Hence, $B(t)$ is bounded in the region Ω_2 such that

$$\Omega_2 = \{B(t) \in \Re_+ : 0 \leq B(t) \leq \eta\tau/\mu(\nu - \alpha)\}$$

Therefore, the feasible solution set of the model (1)-(10) is the region Ω, defined as

$$\Omega = \Omega_1 \times \Omega_2 = \{(S,\quad I_c,\quad R,\quad B) \in \Re_+^4 : 0 \leq N_T(t) \leq (\tau/\mu) + \eta\tau/\mu(\nu - \alpha)\}$$

3.2 *Existence and uniqueness of a solution*

Theorem 3.2 The solution of a formulated Model (11)-(14) exists and unique.

Proof Let us consider the model (11)-(14) as functions.

(i) We can write (11) as follows:
let $dS/dt = f_1(S,\ t) = \tau - \frac{\beta_c BS}{\kappa+B} - \mu S$. Clearly, $f_1(S,\ t)$ and its partial derivative with respect to variable S are continuous. Further, observe that,

$$\begin{aligned} |f_1(S_1,t) - f_1(S_2,t)| &= \left| -\frac{\beta_c BS_1}{\kappa+B} - \mu S_1 + \frac{\beta_c BS_1}{\kappa+B} + \mu S_2 \right| \\ &= \left| -(S_1 - S_2)\left(\frac{\beta_c B}{\kappa+B} + \mu\right)\right| \\ &\leq M|s_1 - s_2| \end{aligned}$$

where, $M = \beta_c + \mu$. Hence, lipschitz condition is satisfied.

(ii) Also, (11) can be rewrittsen as follows:
Let $dI_c/dt = f_2(I_c,t) = \frac{\beta_c BS}{\kappa+B} - (\omega + \delta_1 + \mu)I_c$. We observed that f_2 and its partial derivative with respect to $I_c$are continuous. To verify lipschitz condition consider,

$$\begin{aligned} |f_2(I_{c1},t) - f_2(I_{c2},t)| &= |-(\omega+\delta_1+\mu)I_{c1} + (\omega+\delta_1+\mu)I_{c2}| \\ &= |-(\omega+\delta_1+\mu)(I_{c1} - I_{c2})| \\ &\leq M|I_{c1} - I_{c2}| \end{aligned}$$

where, $M = 2(\omega + \delta_1 + \mu)$. Hence, lipischitz condition is satisfied.
Similarly, the remaining expressions can be proved. Hence, by Cauchy-Lipschitz theorem we can conclude that the formulated model has unique solution for all positive time t.

3.3 *Positivity of solutions*

Theorem 3.3 The solutions of the model (11)-(14) together with the initial conditions $S(0) \geq 0,\ I_c(0) \geq 0,\ R(0) \geq 0,\ B(0) \geq 0$ are always non-negative (OR) the model variables $S,\ I_c,\ R$ and B are non-negative for all t and will remain in $\mathbb{R}^4_+$.

Proof Positivity of the solutions of model equations is shown separately by showing the positivity of each variables $S,\ I_c,\ R$ and B .

Positivity of $S(t)$: Consider the first equation of model (11)-(14),

$$dS/dt = \tau - \frac{\beta_c BS}{\kappa+B} - \mu S.$$

Now excluding the positive term τ, that appearing on the right hand side, we get an inequality $dS/dt \geq -\frac{\beta_c BS}{\kappa+B} - \mu S$. Now solving the foregoing differential inequality we obtain, $S(t) \geq S(0)e^{-\mu t - \int\left[\frac{\beta_c B}{\kappa+B}\right]dt}$. Since the exponential expression $e^{-\mu t - \int\left[\frac{\beta_c B}{\kappa+B} + \beta_h I_h\right]dt}$ is a non-negative quantity, it can be concluded that $S(t) \geq 0$.

Positivity of $I_c(t)$: Consider the second equation of model (11)-(14),

$$dI_c/dt = \frac{\beta_c BS}{\kappa+B} - (\omega + \delta_1 + \mu)I_c\ .$$

Now, excluding the positive term $\frac{\beta_c BS}{\kappa+B}$ we get an inequality $dS/dt \geq -(\omega + \delta_1 + \mu)I_c$. Solving the foregoing differential inequality we get $I_c(t) \geq I_c(0)e^{-(\omega+\delta_1+\mu)t}$. Moreover,

the exponential expression $e^{-(\omega+\delta_1+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $I_c(t) \geq 0$.

Positivity of $R(t)$: Consider the third equation of model (11)-(14),

$$dR/dt = \omega I_c - \mu R .$$

Excluding the positive term ωI_c , we obtain an inequality of the form $dR/dt \geq -\mu R$. Now solving foregoing differential inequality we get $R(t) \geq R(0)e^{-\mu t}$. Further, exponential expression $e^{-\mu t}$ is a non-negative quantity. Hence, it can be concluded that $R(t) \geq 0$.

Positivity of $B(t)$: Consider equation (14) of model (11)-(14),

$$dB/dt = \alpha B + \eta I_c - \nu B.$$

Now, without loss of generality and after excluding the positive term, $\alpha B + \eta I_c$, we get an inequality, $dB/dt \geq -\nu B$. Also solving foregoing differential inequality we get $B(t) \geq B_0 e^{-\nu t}$. Moreover, $e^{-\nu t}$ is a non-negative quantity for all time t . Hence, it can be concluded that $B(t) \geq 0$.
Thus, all solutions of the model are non-negative. Futheremore, the formulated model is biologically meaningful and mathematically well-posed.

3.4 *Equilibrium points*

In order to understand the dynamical behavior of the model, it is necessary to compute equilibrium points of the model. An equilibrium point is a steady state solution of the model (11) – (14) in the sense that if the system start at such state, it will stay there for all times. In other words, the population sizes remain unchanged. Thus, the rate of change of size of a population with respect to a time vanishes. In this subsection we compute disease free equilibrium and endemic equilibrium points.

3.4.1 Disease free equilibrium point

Disease free equilibrium point is a steady state solution where there is no disease in the population. Now, setting $I_c = B = 0$ in model (11)-(14) we obtain the following equation.

$$\tau - \mu S = 0$$

Solving we get $S = S^0 = \frac{\tau}{\mu}$. Thus, the disease free equilibrium E_0 is given by

$$E_0 = (S^0, \quad 0, \quad 0, \quad 0)$$

3.4.2 Endemic equilibrium point

An endemic equilibrium point is steady state point where disease persist in the population. At endemic equilibrium point disease compartment of the model never be zero, but the rate of change of size of each state variable is zero. That is,

$$\tau - \frac{\beta_c BS}{\kappa + B} - \mu S = 0$$
$$\frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu) I_c = 0$$
$$\omega I_c - \mu R = 0$$

$$\alpha B + \eta I_c - \nu B = 0$$

Now solving preceding equations we get $S = \frac{\tau(\beta_c+\mu R_0)}{\mu R_0(\beta_c+\mu)} = S^1$, $I_c = \frac{\mu\kappa(\nu-\alpha)(R_0-1)}{\eta(\beta_c+\mu)} = I_c^1$, $R = \frac{\omega\kappa(\nu-\alpha)(R_0-1)}{\eta(\beta_c+\mu)} = R^1$, $B = \frac{\mu\kappa(R_0-1)}{\beta_c+\mu} = B^1$.

Thus, the endemic equilibrium point $E_c^1 = (S^1, \quad I_c^1, \quad R^1, \quad B^1)$ is given by

$$E_c^1 = \left(\frac{\tau(\beta_c + \mu R_0)}{\mu R_0(\beta_c + \mu)}, \quad \frac{\mu(\nu - \alpha)(R_0 - 1)}{\eta(\beta_c + \mu)}, \quad \frac{\omega\mu(\nu - \alpha)(R_0 - 1)}{\mu\eta(\beta_c + \mu)}, \quad \frac{\mu\kappa(R_0 - 1)}{\beta_c + \mu}\right)$$

3.5 *Basic reproduction number*

The basic reproduction number is defined as the expected number of people getting secondary infection because of infected person enters into wholly susceptible population. The basic reproductive number R_0 is obtained from the computation of next generation matrix. The largest eigenvalue of the next generation matrix is known as basic reproductive number. The formulation of next generation matrix involves classification of all compartments of the model in to two classes: infected and non-infected.

Let f be a matrix consists of newly infected cases and v be a matrix consists of transition cases in model (11)-(14) . Consider model (11)-(14)

$$\begin{aligned} dS/dt &= \tau - \frac{\beta_c BS}{\kappa + B} - \mu S \\ dI_c/dt &= \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu) I_c \\ dR/dt &= \omega I_c - \mu R \\ dB/dt &= \alpha B + \eta I_c - \nu B \end{aligned}$$

Now f and v are given respectively as,

$$f = \begin{bmatrix} \frac{\beta_c BS}{\kappa + B} \\ 0 \end{bmatrix}, \quad v = \begin{bmatrix} (\omega + \delta_1 + \mu) I_c \\ -\alpha B - \eta I_c + \nu B \end{bmatrix},$$

The Jacobian of f and v evaluated at disease free equilibrium point E_0 is given by F and V respectively as follows,

$$F = \begin{bmatrix} 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \omega + \delta_1 + \mu & 0 \\ -\eta & \nu - \alpha \end{bmatrix}$$

The next generation matrix, FV^{-1} is computed and given by

$$FV^{-1} = \begin{bmatrix} \frac{\eta\beta_c S^0}{\kappa(\nu - \alpha)(\delta_1 + \omega + \mu)} & \frac{\beta_c S^0}{\kappa(\delta_1 + \omega + \mu)} \\ 0 & 0 \end{bmatrix}$$

The eigenvalues of next generation matrix are computed and given by,

$$\lambda_1 = \frac{\eta\beta_c S^0}{\kappa(\nu-\alpha)(\delta_1+\omega+\mu)}, \ \lambda_2 = 0 \text{ with } \nu > \alpha.$$

Since reproduction number R_0 is the largest eigenvalue of next generation matrix, it is given by,

$$R_{0c} = \frac{\eta\beta_c S^0}{\kappa(\nu - \alpha)(\delta_1 + \omega + \mu)} \tag{15}$$

3.6 *Stability analysis of the disease free equilibrium point*

In absence of the disease, the model (11)-(14) have a unique disease free equilibrium point E_0 . It is already computed that the DFE of model (11)-(14) is given by (14). Now, the stability analysis of DFE is performed as follows.

3.6.1 Local stability of disease free equilibrium point

Theorem 3.4 If the basic reproduction number (or threshold quantity) R_{0c} is less than one, then disease free equilibrium E_0^c of Cholera model (11)- (14) is unstable.

Proof Consider the model (11)-(14) so that Jacobian matrix of the system at DFE is given by

$$J = \begin{bmatrix} -\mu & 0 & 0 & -\frac{\tau\beta_c}{\mu\kappa} \\ 0 & -(\omega+\delta_1+\mu) & 0 & \frac{\tau\beta_c}{\mu\kappa} \\ 0 & \omega & -\mu & 0 \\ 0 & \eta & 0 & \alpha-\nu \end{bmatrix}$$

Now mathematical computations gives the trace and determinant of the matrix as follows:

$$\text{Trace}\,(J) = -\mu-(\omega+\delta_1+\mu)-\mu+\alpha-\nu<0\ ,$$
$$\text{Det}\,(J) = (\nu-\alpha)\big((\omega+\delta_1+\mu)\big)\mu^2(1-R_{0c}) > 0$$

Here it can observed that, trace of a Jacobian matrix is less than zero and determinant of a matrix is greater than zero if $R_0 < 1$. Hence, by using trace-determinant principle we conclude that DFE is locally asymptotically stable if $R_0 < 1$.

3.6.2 Local stability of endemic equilibrium point

Theorem 3.5 Let R_{0c} be basic reproduction number of Cholera model (11)-(14). Then the endemic equilibrium E_1^c is locally asymptotically stable if $1 < R_{0c} < \left(1+\frac{B^1}{\kappa}\right)^2$.

Proof Consider the model (11)-(14) so that Jacobian matrix of the system at E_1^c is given by

$$J = \begin{bmatrix} -\mu & 0 & 0 & -\frac{\beta_c\kappa S^1}{(\kappa+B^1)^2} \\ 0 & -(\omega+\delta_1+\mu) & 0 & \frac{\beta_c\kappa S^1}{(\kappa+B^1)^2} \\ 0 & \omega & -\mu & 0 \\ 0 & \eta & 0 & \alpha-\nu \end{bmatrix}$$

Now, mathematical computations gives the trace and determinant of the matrix as follows:

$$\text{Trace}\,(J) = -\mu-(\omega+\delta_1+\mu)-\mu+\alpha-\nu,$$
$$\text{Det}\,(J) = \mu^2\left(1-\left(\frac{\kappa}{\kappa+B^1}\right)^2 R_0\right).$$

Here it can be observed that, trace of a Jacobian matrix is less than zero and determinant of a matrix is greater than zero if $\left(\frac{\kappa}{\kappa+B^1}\right)^2 R_0 < 1 \Rightarrow R_0 < \left(\frac{\kappa+B^1}{\kappa}\right)^2$. Hence, by using trace-determinant principle we conclude that endemic equilibrium is locally asymptotically stable if $R_0 < 1$.

3.6.3 Global stability of disease free equilibrium point

To show global stability we follow the procedures given in [6, 1] . That is, let $x \in R^2$ is disease compartment and $y \in R^2$ be disease free compartment. The disease transmission model (11)- (14) can be written in the form:

$$\dot{x} = -(V - F)x - h(x, y), \qquad \dot{y} = g(x, y),$$

where, $x = (I_c, \quad B)$ and $y = (S, \quad R)$. Further, F and V are given in subsection 3.5.

Theorem 3.6 Let $V - F$ is a non-singular M-matrix and $h \geq 0$. Then a disease-free equilibrium of model (11)-(14) is globally asymptotically stable if $R_0 < 1$.

Proof Now, the rate of change of the variables in the model equations (11)-(14) can be rewritten as

$$\dot{x} = -(V - F)x - \left[\left(\frac{\beta S_0}{\kappa} - \frac{\beta S}{\kappa + B}\right)\right]$$
$$\dot{S} = \tau - \frac{\beta_c B S}{\kappa + B} - \mu S$$
$$\dot{R} = \omega I_c - \mu R$$

where F and V are computed in subsection 3.5 and given by

$$F = \begin{bmatrix} 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & 0 \end{bmatrix}, V = \left[\begin{bmatrix} \omega + \delta_1 + \mu & 0 \\ -\eta & \nu - \alpha \end{bmatrix}\right]$$

Consider $V - F = \begin{bmatrix} \omega + \delta_1 + \mu & -\frac{\beta_c S^0}{\kappa} \\ -\eta & \nu - \alpha \end{bmatrix} = sI - B$. Where, $s = \max\{\omega + \delta_1 + \mu, \nu - \alpha\}$ and $B = \begin{bmatrix} 0 & \frac{\beta_c S^0}{\kappa} \\ \eta & 0 \end{bmatrix}$. Thus, $V - F$ has Z sign pattern. Further, $\det(V - F) = (\omega + \delta_1 + \mu)(\nu - \alpha) - \eta\left(\frac{\beta_c S^0}{\kappa}\right) = (\omega + \delta_1 + \mu)(\nu - \alpha)(1 - R_0) > 0$ if $R_0 < 1$. Thus, $V - F$ is non-singular matrix if $R_0 < 1$. Now it follows that $V - F$ is non-singular M–matrix if $s > \rho(B) = \sqrt{\frac{\eta \beta_c S^0}{\kappa}}$. Next, we want show that $h(x, y) \geq 0$. Consider $h(x, y) = \left[\left(\frac{\beta S_0}{\kappa} - \frac{\beta S}{\kappa + B}\right)\right]$. At disease free equilibrium, we observe that $S(t) \longrightarrow S_0$ as $t \longrightarrow \infty$. Hence, $h(x, y) \longrightarrow \mathbf{0}$ as $(S, \quad I_c, \quad R, \quad B) \longrightarrow (S_0, \quad 0, \quad 0, \quad 0)$. Therefore, taking $h(x, y) = \mathbf{0}$ and using the above hypothesis the disease-free equilibrium point of model (11) – (14) is globally asymptotically stable for $R_0 < 1$.

4. Mathematical analysis of HIV only model

The HIV only model follows from the model (1)-(10) by setting $I_c = I_{hc} = A_c = 0$. Then we get:

$$dS/dt = \tau - \beta_h S I_h - \mu S \tag{16}$$
$$dI_h/dt = \beta_h S I_h - (\gamma + \mu) I_h \tag{17}$$

$$dA/dt = \gamma I_h \ - (\delta_3 + \mu)A \tag{18}$$

With $S(0) \geq 0,\ I_h(0) \geq 0,\ A(0) \geq 0$.

4.1 *Invariant region*

Theorem 4.1 The model (16)-(18) has a bounded solution in the region Ω for all $t > 0$.

Proof Let $x = (S,\ \ I_h,\ \ A) \in \Re_+^4$ represents a solution of a model (16)-(18) with the given initial conditions in the invariant region. let Ω_1 be invariant region that consists of three solution variables of human population with the given initial conditions. Moreover, consider total size of human population, $N(t)$, at time t which is given by

$$N(t) = S(t) + I_h(t) + A(t) \tag{19}$$

Now differentiating both sides of (19) with respect to time t we get

$$\begin{aligned} &\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_h}{dt} + \frac{dA}{dt} \\ &\Rightarrow \frac{dN}{dt} = \tau - \mu N - \delta_2 A \leq \tau - \mu N \\ &\Rightarrow dN/dt \leq \tau - \mu N \\ &\Rightarrow dN/(\tau - \mu N) \leq dt \end{aligned} \tag{20}$$

Integrating both sides of (20) over $[0\ , t]$ we have,

$$\begin{aligned} &\int_0^t \frac{1}{\tau - \mu N} dN \leq \int_0^t dt \\ &\Rightarrow \ \tfrac{\tau - \mu N(t)}{\tau - \mu N(0)} \geq e^{-\mu t} \ \ [\text{ Assuming } N(0) < \tfrac{\tau}{\mu} \ ] \\ &\Rightarrow \tau - \mu N(t) \ \ \geq \big(\tau - \mu N(0)\big)e^{-\mu t} \\ &\Rightarrow N(t) \leq (\tau/\mu) - \big(\tau/\mu - N(0)\big)e^{-\mu t} \end{aligned} \tag{21}$$

Now as $t \longrightarrow \infty$ (21) reduced to the form,

$$N(t) \leq \tau/\mu \tag{22}$$

Now using (22) and general biological truth about human population, we have, $0 \leq N(t) \leq \tau/\mu$. Thus, all solution variables of human population are bounded in Ω_1 . That is,

$$\Omega_1 = \big\{\big((S,\ \ I_h,\ \ A) \in \Re_+^3\big) \in \Re_+^3 \colon 0 \leq N(t) \leq \tau/\mu \ \big\}.$$

4.2 *Existence and uniqueness of a solution*

Theorem 4.2 The solution of a formulated Model (16)-(18) exists and unique.

Proof Let us consider the model (16)-(18) as functions. We can write (16) as follows:

Let $dS/dt = f_1(S,\ t) = \tau - \beta_h S I_h - \mu S$. Clearly, $f_1(S,\ t)$ and its partial derivative with respect to a variable S are continuous. Further, observe that,

$$\begin{aligned} |f_1(S_1, t) - f_1(S_2, t)| &= |\ -\beta_h S_1 I_h - \mu S_1 + \beta_h S_2 I_h + \mu S_2\ | \\ &= |-(S_1 - S_2)(\beta_h I_h\ + \mu)| \\ &\leq M|s_1 - s_2| \end{aligned}$$

where, $M = \frac{\beta_h \tau}{\mu} + \mu$. Hence, lipschitz condition is satisfied.

Similarly, the remaining expressions can be proved. Hence, by Cauchy-Lipschitz theorem we can conclude that the formulated HIV only model has unique solution for all positive time t.

4.3 *Positivity of solutions*

Theorem 4.3 The solutions of the model (16)-(18) together with the given the initial conditions $S(0) \geq 0$, $I_h(0) \geq 0$, $A(0) \geq 0$ are always non-negative (OR) the model variables S, I_h and A are non-negative for all t and remain in $\mathbb{R}^3_+$.

Proof Positivity of the solutions of model equations follows from the positivity of each variables S, I_h, and A .

Positivity of $S(t)$: Consider the first equation of model (16)-(18),

$$\begin{aligned} &dS/dt = \tau - \beta_h S I_h - \mu S \\ &\Rightarrow dS/dt \geq -\beta_h S I_h - \mu S \\ &\Rightarrow S(t) \geq S(0) e^{-\mu t - \beta_h \int I_h dt} \end{aligned}$$

Since the exponential expression $e^{-\mu t - \beta_h \int I_h dt}$ is a non-negative quantity, it can be concluded that $S(t) \geq 0$.

Positivity of $I_h(t)$: Consider the second equation of the model (16)-(18),

$$\begin{aligned} &dI_h/dt = \beta_h S I_h - (\gamma + \mu) I_h \\ &\Rightarrow dI_h/dt \geq -(\gamma + \mu) I_h \\ &\Rightarrow I_h(t) \geq I_h(0) e^{-(\gamma+\mu)t} \end{aligned}$$

Moreover, the exponential expression $e^{-((\gamma+\mu))t}$ is a non-negative quantity. Hence, it can be concluded that $I_h(t) \geq 0$.

Positivity of $A(t)$: Consider the third equation of model (16)-(18),

$$\begin{aligned} &dA/dt = \gamma I_h - (\delta_3 + \mu) A \\ &\Rightarrow dA/dt \geq -(\delta_3 + \mu) A \\ &\Rightarrow A(t) \geq A(0) e^{-(\delta_3+\mu)t} \end{aligned}$$

Further, exponential expression $e^{-(\delta_3+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $A(t) \geq 0$.

Thus, all solutions of the model are non-negative. Futheremore, the formulated model is biologically meaningful and mathematically well-posed.

4.4 *Equilibrium points*

4.4.1 Disease free equilibrium point

Disease free equilibrium point (DFE) is a steady state solution where there is no disease in the population. Now, setting $I_c = B = 0$ in model (16)-(18) we obtain the following equation

$$\tau - \mu S = 0.$$

Solving we get $S = S^0 = \frac{\tau}{\mu}$. Thus, the disease free equilibrium E_0 is given by

$$E_0 = (S^0, \quad 0, \quad 0) .$$

4.4.2 Endemic equilibrium point

An endemic equilibrium point is steady state point where disease persist in the population. At endemic equilibrium point disease compartment of the model never be zero, but the rate of change of size of each state variable is zero. That is,

$$dS/dt = \tau - \beta_h S I_h - \mu S$$
$$dI_h/dt = \beta_h S I_h - (\gamma + \mu) I_h$$
$$dA/dt = \gamma I_h - (\delta_3 + \mu) A$$

Now, solving preceding equations we get $S = \frac{\gamma+\mu}{\beta_h} = S^1$, $I_h^1 = \frac{\tau\beta_h - \mu(\gamma+\mu)}{\beta_h(\gamma+\mu)}$, $A^1 = \frac{\gamma}{\delta_3+\mu}$. Thus, the endemic equilibrium point $E_h^1 = (S^1, \quad I_h^1, \quad A^1)$ is given by

$$E_h^1 = \left(\frac{\tau}{\mu R_{h0}}, \quad \frac{\mu(R_{0h}-1)}{\beta_h}, \quad \frac{\gamma}{\delta_3+\mu}\right).$$

4.5 ***Basic reproduction number***

The basic reproduction number is defined as the expected number of people getting secondary infection because of infected person enters into wholly susceptible population. The basic reproductive number R_0 is obtained from the computation of next generation matrix. The largest eigenvalue of the next generation matrix is known as basic reproductive number. The formulation of next generation matrix involves classification of all compartments of the model in to two classes: infected and non-infected.

Let f be a matrix consists of newly infected cases and v be a matrix consists of transition cases in model (16)-(18). Consider model (16)-(18)

$$dS/dt = \tau - \beta_h S I_h - \mu S$$
$$dI_h/dt = \beta_h S I_h - (\gamma + \mu) I_h$$
$$dA/dt = \gamma I_h - (\delta_3 + \mu) A$$

Now, f and v are given respectively as,

$$f = \begin{bmatrix} \beta_h S I_h \\ 0 \end{bmatrix}, \qquad v = \begin{bmatrix} (\gamma+\mu) I_h \\ -\gamma I_h + (\delta_3+\mu) A \end{bmatrix}.$$

The Jacobean of f and v evaluated at disease free equilibrium point E_0 is given by F and V respectively as follows,

$$F = \begin{bmatrix} \beta_h S^0 & 0 \\ 0 & 0 \end{bmatrix}, \qquad V = \begin{bmatrix} \gamma+\mu & 0 \\ -\gamma & \delta_3+\mu \end{bmatrix}.$$

The next generation matrix, FV^{-1} is computed and given by

$$FV^{-1} = \begin{bmatrix} \frac{\beta_h S^0}{\gamma+\mu} & 0 \\ 0 & 0 \end{bmatrix}.$$

The eigenvalues of next generation matrix are computed and given by,

$$\lambda_1 = \frac{\beta_h S^0}{\gamma+\mu}, \quad \lambda_2 = 0.$$

Since reproduction number R_{0h} is the largest eigenvalue of next generation matrix, it is given by,

$$R_{0h} = \frac{\beta_h S^0}{\gamma+\mu}. \tag{22}$$

4.6 *Stability analysis of the disease free equilibrium point*

In absence of the disease, the model (16)-(18) have a unique disease free equilibrium point E_0 . The DFE of model (16)-(18) is already computed and given by $E_0^h = \frac{\tau}{\mu}$. Now, the stability analysis of DFE is performed as follows.

4.6.1 Local stability of disease free equilibrium point

Theorem 4.4 If the basic reproduction number (or threshold quantity) R_{0h} is less than one, then disease free equilibrium E_0^h of Cholera model (16)-(18) is unstable.

Proof Consider the model (16)-(18) so that Jacobian matrix of the system at DFE is given by

$$J = \begin{bmatrix} -\mu & -\beta_h(\tau/\mu) & 0 \\ 0 & \beta_h(\tau/\mu) - (\gamma+\mu) & 0 \\ 0 & \gamma & -(\delta_3+\mu) \end{bmatrix}$$

Now mathematical computations gives eigenvalues of Jacobean matrix J as follows:

$$\lambda_1 = -\mu\,,\ \lambda_2 = (\gamma+\mu)(R_0-1),\ \lambda_3 = -(\delta_3+\mu).$$

Here, it can be observed that, all eigenvalues of Jacobian matrix is less than zero if $R_0 < 1$. Hence, by linearity principle the DFE is locally asymptotically stable if $R_0 < 1$.

4.6.2 Global stability of disease free equilibrium point

Let $x \in R^2$ is disease compartment and $y \in R^1$ be disease free compartment. The disease transmission model (16)-(18) can be written in the form:

$$\dot{x} = -(V-F)x - h(x,y)$$
$$\dot{y} = g(x,y)$$

where, $x = (I_h,\quad A)$ and $y = S$. Further, F and V are given in subsection 4.5.

Theorem 4.5 Let $V-F$ is a non-singular M-matrix and $h \geq 0$. Then a disease-free equilibrium of model (16)-(18) is globally asymptotically stable if $R_0 < 1$.

Proof The rate of change of the variables in the model equations (16)-(18) can be rewritten as

$$\dot{x} = -(V-F)x - \beta_h(S^0 - S)$$
$$\dot{S} = \tau - \beta_h I_h S - \mu S$$

The computed F and V are given by

$$F = \begin{bmatrix} \beta_h S^0 & 0 \\ 0 & 0 \end{bmatrix},\quad V = \begin{bmatrix} \gamma+\mu & 0 \\ -\gamma & \delta_3+\mu \end{bmatrix}$$

Consider $V - F = \begin{bmatrix} \gamma+\mu-\beta_h S^0 & 0 \\ -\gamma & \delta_3+\mu \end{bmatrix} = sI - B$. Where, $s = \max\{\gamma+\mu, \delta_3+\mu\}$ and $B = \begin{bmatrix} \beta_h S^0 & 0 \\ 0 & 0 \end{bmatrix}$. Thus, $V-F$ has Z sign pattern. Further, $\det(V-F) = (\gamma+\mu)(1-R_{0h}) > 0$ if $R_0 < 1$. Thus, $V-F$ is non-singular matrix if $R_0 < 1$. Now it follows that $V-F$ is non-singular M–matrix if $s > \rho(B) = \beta_h S^0$. Next, we want show

that $h(x,\ y) \geq 0$. Consider $h(x,\ y) = \beta_h S^0$. At disease free equilibrium, we observe that $S(t) \longrightarrow S_0$ as $t \longrightarrow \infty$. Hence, $h(x,\ y) \longrightarrow \mathbf{0}$ as $(S,\ \ I_h,\ \ A) \longrightarrow (S_0,\ \ 0,\ \ 0)$. Therefore, taking $h(x,\ y) = \mathbf{0}$ and using the above hypothesis the disease-free equilibrium point of model (16)-(18) is globally asymptotically stable for $R_0 < 1$.

5. Mathematical analysis of HIV– Cholera model

5.1 *Invariant region*

Theorem 5.1 The solutions of the model (1)-(10) are bounded for all $t > 0$ if they enter invariant region $\Omega = \Re_+^{10}$.

Proof Let $\mathrm{x} = (S,\ \ I_c,\ \ R,\ \ I_h,\ \ I_{hc},\ \ A,\ \ A_c,\ \ R_h,\ \ R_A) \in \Re_+^{10}$ be a solution of model (1)-(10) with initial conditions in the invariant region Ω. We divide total population into two categories: Human population and Bacteria population. Let $N_T(t)$ be total population size at time t such that

$$N_T(t) = N(t) + B(t)$$

Where, $N(t)$ be the size of total human population and $B(t)$ be the size of bacteria population.

Now, (i) let Ω_1 be invariant region consisting of nine solution variables that represents human population with initial conditions. Moreover, let total human population size, $N(t)$, at time t is given by

$$N(t) = S(t) + I_c(t) + R(t) + I_h(t) + I_{hc}(t) + A(t) + A_c(t) + R_h(t) + R_A(t) \qquad (24)$$

Now, differentiating both sides of equation (5) with respect to time t we have

$$\begin{aligned}
&\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI_c}{dt} + \frac{dR}{dt} + \frac{dI_h}{dt} + \frac{dI_{hc}}{dt} + \frac{dA}{dt} + \frac{dA_c}{dt} + \frac{dR_h}{dt} + \frac{dR_A}{dt} \\
&\Rightarrow \frac{dN}{dt} = \tau - \mu N - \delta_1 I_c - \delta_2 I_{hc} - \delta_3 A - \delta_4 A_c - \delta_5 R_A \leq \tau - \mu N \\
&\Rightarrow dN/dt \leq \tau - \mu N \\
&\Rightarrow dN/(\tau - \mu N) \leq dt
\end{aligned} \qquad (25)$$

Integrating both sides of (25) over $[0\ t]$ we have,

$$\begin{aligned}
&\int_0^t \frac{1}{\tau - \mu N} dN \leq \int_0^t dt \\
&\Rightarrow ln|\tau - \mu N|_0^t \geq -\mu t \\
&\Rightarrow ln\left|\frac{\tau - \mu N(t)}{\tau - \mu N(0)}\right| \geq -\mu t \\
&\Rightarrow \left|\frac{\tau - \mu N(t)}{\tau - \mu N(0)}\right| \geq e^{-\mu t} \\
&\Rightarrow \frac{\tau - \mu N(t)}{\tau - \mu N(0)} \geq e^{-\mu t} \quad [\text{Assuming } N(0) < \tfrac{\tau}{\mu}] \\
&\Rightarrow \tau - \mu N(t) \geq \big(\tau - \mu N(0)\big)e^{-\mu t} \\
&\Rightarrow \tau - \big(\tau - \mu N(0)\big)e^{-\mu t} \geq \mu N(t) \\
&\Rightarrow N(t) \leq (\tau/\mu) - \big(\tau/\mu - N(0)\big)e^{-\mu t}
\end{aligned} \qquad (26)$$

Now as $t \longrightarrow \infty$ equation (26) reduced to the form,

$$N(t) \leq \tau/\mu \tag{27}$$

Now using (27) and general truth about population, we have, $0 \leq N(t) \leq \tau/\mu$. Thus, all solution variables of human population are bounded in Ω_1 . That is,

$$\Omega_1 = \{(S,\ \ I_c,\ \ R,\ \ I_h,\ \ I_{hc},\ \ A,\ \ A_c,\ \ R_h,\ \ R_A) \in \Re_+^9 : 0 \leq N(t) \leq \tau/\mu\ \}$$

Similarly, let $B(t)$ be population size of bacterial population, with bounded initial conditions. Now considering boundedness of state variables, that represent human population, (6) gives,

$$\begin{aligned} &dB/dt = \alpha B + \eta I_c - \nu B \\ &\Rightarrow dB/B + \tau/\mu \leq dt \\ &\Rightarrow dB/(\alpha - \nu)B + \tau/\mu \leq (\alpha - \nu)t \end{aligned} \tag{28}$$

Integrating both sides of (28) over [0,t] and assuming $0 < \alpha < \nu$, we get,

$$B(t) = \tau/\mu(\nu - \alpha) - (B_0 + \tau/\mu(\nu - \alpha))e^{-(\nu-\alpha)t} \tag{29}$$

Now as $t \longrightarrow \infty$ equation (29) reduced to the form,

$$B(t) \leq \tau/\mu(\nu - \alpha)$$

Hence, $B(t)$ is bounded in the region Ω_2 such that

$$\Omega_2 = \{B(t) \in \Re_+ : 0 \leq B(t) \leq \tau/\mu(\nu - \alpha)\ \} \tag{30}$$

Therefore, the feasible solution set of the model (1)-(10) is the region Ω , defined as

$$\begin{aligned} \Omega = \Omega_1 \times \Omega_2 = \{&(S,\ \ I_c,\ \ R,\ \ I_h,\ \ I_{hc},\ \ A,\ \ A_c,\ \ R_h,\ \ R_A,\ \ B) \in \Re_+^{10} : 0 \leq N_T(t) \\ &\leq \tau/\mu + \tau/\mu(\nu - \alpha)\ \} \end{aligned}$$

5.2 Existence and Uniqueness of a Solution

Theorem 5.2 The solution of a model (1)-(10) with initial conditions exist and unique.

Proof let us consider the model (1)-(10) as functions.

(i) The first equation of model (1)-(10) can be written in the function form as follows:

Let $dS/dt = f_1(S,\ t) = \tau - \frac{\beta_c BS}{\kappa + B} - \beta_h S I_h - \mu S$. Clearly, $f_1(S,\ t)$ and its partial derivative with respect to variable S are continuous. Further, observe that,

$$\begin{aligned} |f_1(S_1, t) - f_1(S_2, t)| &= \left| -\frac{\beta_c BS_1}{\kappa + B} - \beta_h S_1 I_h - \mu S_1 + \frac{\beta_c BS_1}{\kappa + B} + \beta_h S_2 I_h + \mu S_2 \right| \\ &= \left| -(S_1 - S_2)\left(\frac{\beta_c B}{\kappa + B} + \beta_h I_h + \mu\right) \right| \\ &\leq M|s_1 - s_2| \end{aligned}$$

where, $M = \beta_c + \beta_h(\tau/\mu) + \mu$. Hence, lipschitz condition is satisfied.

(ii) The second equation of model (1)-(10) can be rewrittsen as as follows:
Let $dI_c/dt = f_2(I_c, t) = \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu)I_c$. Here, f_2 and its partial derivative with respect to I_c are continuous. Le consider the following expression to verify lipschitz condition.

$$|f_2(I_{c1}, t) - f_2(I_{c2}, t)| = |-(\omega + \delta_1 + \mu)I_{c1} + (\omega + \delta_1 + \mu)I_{c2}|$$

$$= |-(\omega + \delta_1 + \mu)(I_{c1} - I_{c2})|$$
$$\leq M|I_{c1} - I_{c2}|$$

where, $M = 2(\omega + \delta_1 + \mu)$. Hence, lipischitz condition is satisfied

(iii) From third equation of model (1)-(10) we have:
$dR/dt = f_3(R,t) = \omega I_c - \mu R$. Here, f_3 and its partial derivatives with respect to R are continuous. On the other hand, consider expression,

$$|f_3(R_1,t) - f_3(R_2,t)| = |-\mu R_1 + \mu R_2|$$
$$= \mu|R_1 - R_2|$$
$$\leq M|R_1 - R_2|$$

where, $M = 2\mu$. Hence, Lipischitz condition is fulfilled.

Similarly, the remaining expressions can be proved. Hence, by Cauchy-Lipschitz theorem we can conclude that the formulated model has unique solution for all positive time t.

5.3 *Positivity of model solutions*

Theorem 5.3 Solutions of the model (1) – (10) together with the initial conditions $S(0) \geq 0,\ I_c(0) \geq 0,\ R(0) \geq 0,\ I_h(0) \geq 0, I_{hc}(0) \geq 0, A(0) \geq 0, A_c(0) \geq 0,\ R_h(t) \geq 0,\ R_A(0) \geq 0,\ B(0) \geq 0$ are always non-negative (OR) the model variables $S,\ I_c,\ R,\ I_h, I_{hc}, A, A_c, R_h,\ R_A$ and B are non-negative for all t and will remain in $\mathbb{R}_+^{10}$.

Proof Positivity of the solutions of model equations is shown separately by showing the positivity of each variables $S,\ I_c,\ R,\ I_h, I_{hc}, A, A_c, R_h,\ R_A$ and B.

Positivity of $S(t)$ *:* Consider the first equation of model (1)-(10),

$$dS/dt = \tau - \frac{\beta_c BS}{\kappa + B} - \beta_h S I_h - \mu S.$$

It can be expressed as, after eliminating the positive term τ that appearing on the right hand side, an inequality $dS/dt \geq -\frac{\beta_c BS}{\kappa + B} - \beta_h S I_h - \mu S$. Using variables separ`ation method and on applying integration, the solution of the foregoing differential inequality can be obtained as $S(t) \geq S(0)e^{-\mu t - \int\left[\frac{\beta_c B}{\kappa + B} + \beta_h I_h\right]dt}$. Recall that an exponential function is always non–negative irrespective of the sign of the exponent i.e., the exponential function $e^{-\mu t - \int\left[\frac{\beta_c B}{\kappa + B} + \beta_h I_h\right]dt}$ is a non-negative quantity. Hence, it can be concluded that $S(t) \geq 0$.

Positivity of $I_c(t)$: Consider the second equation of model (1)-(6),

$$dI_c/dt = \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu)I_c.$$

It can be expressed as, after eliminating the positive term $\frac{\beta_c BS}{\kappa + B}$ that appearing on the right hand side, an inequality $dS/dt \geq -(\omega + \delta_1 + \mu)I_c$. Using variables separation method and on applying integration, the solution of the foregoing differential inequality can be obtained as $I_c(t) \geq I_c(0)e^{-(\omega + \delta_1 + \mu)t}$. Recall that an exponential function is always non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\omega + \delta_1 + \mu)t}$ is a non-negative quantity. Hence, it can be concluded that $I_c(t) \geq 0$.

Positivity of $R(t)$: Consider the third equation of model (1)-(10),

$$dR/dt = \omega I_c - \mu R.$$

It can be expressed as, after eliminating the positive term ωI_c, that appearing on the right hand side, we obtain an inequality $dR/dt \geq -\mu R$. Using variables separation method and on applying integration, the solution of the foregoing differential inequality can be obtained as $R(t) \geq R(0)e^{-\mu t}$. Recall that an exponential function is always non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-\mu t}$ is a non-negative quantity. Hence, it can be concluded that $R(t) \geq 0$.

Positivity of $I_h(t)$: Consider the equation (4) of model (1)-(10). That is,

$$dI_h/dt = \beta_h S I_h - \frac{\beta_c B I_h}{\kappa + B} - (\gamma + \mu) I_h.$$

After eliminating the positive term $\beta_h S I_h$ which is appearing on the right hand side, it can be expressed as inequality $dI_h/dt \geq -\frac{\beta_c B I_h}{\kappa + B} - (\gamma + \mu) I_h$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality can be obtained as $dI_h/dt \geq I_h(0)\, e^{-(\gamma+\mu)t - \beta_c \int \frac{B}{\kappa+B} dt}$. Recall that an exponential function is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\gamma+\mu)t - \beta_c \int \frac{B}{\kappa+B} dt}$ is a non-negative quantity. Hence, it can be concluded that $I_h(t) \geq 0$.

Positivity of $I_{hc}(t)$: Consider the equation (5) of model (1)-(10). That is,

$$dI_{hc}/dt = \frac{\beta_c B I_h}{\kappa + B} - (\rho + \sigma + \delta_2 + \mu) I_{hc}.$$

After eliminating the positive term $\frac{\beta_c B I_h}{\kappa + B}$ which is appearing on the right hand side, it can be expressed as inequality $dI_{hc}/dt \geq -(\rho + \sigma + \delta_2 + \mu) I_{hc}$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality is, $I_{hc} \geq I_{hc}(0) e^{-(\rho+\sigma+\delta_2+\mu)t}$. Recall that an exponential function is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\rho+\sigma+\delta_2+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $I_{hc}(t) \geq 0$.

Positivity of $A(t)$: Consider the equation (6) of model (1)-(10). That is,

$$dA/dt = \gamma I_h - \frac{\beta_c B A}{\kappa + B} - (\delta_3 + \mu) A.$$

After eliminating the positive term γI_h, which is appearing on the right hand side, it can be expressed as inequality $dA/dt \geq -\frac{\beta_c B A}{\kappa + B} - (\delta_3 + \mu) A$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality is, $A(t) \geq A(0) e^{-(\delta_3+\mu)t - \beta_c \int \frac{B}{\kappa+B}\, dt}$. Recall that an exponential function is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\delta_3+\mu)t - \beta_c \int \frac{B}{\kappa+B}\, dt}$ is a non-negative quantity. Hence, it can be concluded that $A(t) \geq 0$.

Positivity of $A_c(t)$: Consider the equation (7) of model (1)-(10). That is,

$$dA_c/dt = \frac{\beta_c B A}{\kappa + B} + \rho I_{hc} - (\phi + \delta_4 + \mu) A_c.$$

After eliminating the positive term $\frac{\beta_c B A}{\kappa + B} + \rho I_{hc}$, which is appearing on the right hand side, it can be expressed as inequality $dA_c/dt \geq -(\phi + \delta_4 + \mu) A_c$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality is, $A_c(t) \geq A_c(0) e^{-(\phi+\delta_4+\mu)t}$. Recall that an exponential function

is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\phi+\delta_4+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $A_c(t) \geq 0$.

Positivity of $R_h(t)$: Consider the equation (8) of model (1)-(10). That is,

$$dR_h/dt = \sigma I_{hc} - (\theta + \mu)R_h.$$

After eliminating the positive term σI_{hc}, which is appearing on the right hand side, it can be expressed as inequality $dR_h/dt \geq -(\theta + \mu)R_h$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality is, $R_h(t) \geq R_h(0)e^{-(\theta+\mu)t}$. Recall that an exponential function is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\theta+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $R_h(t) \geq 0$.

Positivity of $R_A(t)$: Consider the equation (9) of model (1)-(10). That is,

$$dR_A/dt = \theta R_h + \phi A_c - (\delta_5 + \mu)R_A.$$

After eliminating the positive term $\theta R_h + \phi A_c$, which is appearing on the right hand side, it can be expressed as inequality $dR_A/dt \geq -(\delta_5 + \mu)R_A$. Now, using variables separation method and on applying integration, the solution of the foregoing differential inequality is, $R_A(t) \geq R_A(0)e^{-(\delta_5+\mu)t}$. Recall that an exponential function is always a non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-(\delta_5+\mu)t}$ is a non-negative quantity. Hence, it can be concluded that $R_A(t) \geq 0$.

Positivity of $B(t)$: Consider equation (10) of model (1)-(10),

$$dB/dt = \alpha B + \eta I_c - \nu B.$$

Now, without loss of generality and after eliminating the positive term $\alpha B + \eta I_c$ which is appearing on the right hand side of equation (10) we have an inequality, $dB/dt \geq -\nu B$. Using variables separation method and on applying integration, the solution of the foregoing differential inequality can be obtained as $B(t) \geq B_0 e^{-\nu t}$. Recall that an exponential function is always non–negative irrespective of the sign of the exponent i.e. the exponential function $e^{-\nu t}$ is a non-negative quantity for all time t. Hence, it can be concluded that $B(t) \geq 0$. Thus, all solutions of the model are non-negative. Futheremore, the formulated model is biologically meaningful and mathematically well-posed.

5.4 *Equilibrium points*

In order to understand the dynamics of the model, it is necessary to determine equilibrium points of the solution region. An equilibrium solution is a steady state solution of the model equations (1)-(10) in the sense that if the system begins at such a state, it will remain there for all times. In other words, the population sizes remain unchanged and thus the rate of change for each population vanishes. Equilibrium points of the model are found, categorized, stability analysis is conducted and the results have been presented in the following sub-sections:

5.4.1 Disease free equilibrium point

Disease free equilibrium point is a steady state solution where there is no disease in the population. Now, setting $I_c = I_h = I_{hc} = A = A_c = R_h = R_A = B = 0$ in model (1)-(10) we obtain the following equation

$$\tau - \mu S = 0.$$

Solving we get $S = S^0 = \frac{\tau}{\mu}$. Thus, the disease free equilibrium E_0 is given by $E_0 = (S^0, \ I_c^0, \ R^0, \ I_h^0, \ I_{hc}^0, \ A^0, \ A_c^0, \ R_h^0, \ R_A^0, \ B^0)$ of the model (1)-(10) is given by

$$E_0 = \left(\frac{\tau}{\mu}, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0\right). \tag{31}$$

5.4.2 Endemic equilibrium point

An endemic equilibrium point is steady state point where disease persist in the population. At endemic equilibrium point disease compartment of the model never be zero, but the rate of change of size of each state variable is zero. That is,

$$\begin{aligned} dS/dt = dI_c/dt = \ dR/dt = dI_h/dt = dI_{hc}/dt = dA/dt = dA_c/dt = \ dR_h/dt = \\ dR_A/dt = \ dB/dt = 0, \\ \tau - \frac{\beta_c BS}{\kappa+B} - \beta_h S I_h - \mu S = 0, \\ \frac{\beta_c BS}{\kappa+B} - (\omega + \delta_1 + \mu) I_c = 0, \\ \omega I_c - \mu R = 0, \\ \beta_h S I_h - \frac{\beta_c B I_h}{\kappa+B} \ - (\gamma + \mu) I_h = 0, \\ \frac{\beta_c B I_h}{\kappa+B} - (\rho + \sigma + \delta_2 + \mu) I_{hc} \ = 0, \\ \gamma I_h - \frac{\beta_c BA}{\kappa+B} - (\delta_3 + \mu) A \ = 0, \\ \frac{\beta_c BA}{\kappa+B} + \rho I_{hc} - (\phi + \delta_4 + \mu) A_c = 0, \\ \sigma I_{hc} - (\theta + \mu) R_h = 0, \\ \theta R_h + \phi A_c - (\delta_5 + \mu) R_A = 0, \\ \alpha B + \eta I_c - \nu B = 0. \end{aligned}$$

Solving the above equations we get:

$$\begin{aligned} S &= \beta_c + \gamma + \mu - \sqrt{(\beta_c + \gamma + \mu)^2 - 4\beta_h(\omega + \delta_{\cdot} + \mu)(\kappa(\nu - \alpha)/\eta)} = S^1, \\ B &= \frac{(\beta_h S^1 - \gamma - \mu)\kappa}{\beta_c - (\beta_h S^1 - \gamma - \mu)} = B^1, \\ I_c &= \frac{(\nu - \alpha)B^1}{\eta} = I_c^1, \\ R &= \frac{\omega I_c^1}{\mu} = R^1, \\ I_h &= \frac{\tau}{\beta_h S^1} - \frac{\beta_c B^1}{\beta_h(\kappa + B^1)} - \frac{\mu}{\beta_h} = I_h^1, \\ I_{hc} &= \frac{\beta_c B^1 I_h^1}{(\kappa + B^1)(\rho + \sigma + \delta_2 + \mu)} = I_{hc}^1, \\ A &= \frac{\gamma I_h^1(\kappa + B^1)}{\beta_c B^1 + (\kappa + B^1)(\delta_3 + \mu)} = A^1, \\ A_c &= \frac{\beta_c B^1 A^1}{(\kappa + B^1)(\phi + \delta_4 + \mu)} + \frac{\rho I_{hc}^1}{(\phi + \delta_4 + \mu)} = A_c^1, \\ R_h &= \frac{\sigma I_{hc}^1}{\theta + \mu} = R_h^1, \\ R_A &= \frac{\theta R_h^1 + \phi A_c^1}{\delta_5 + \mu} = R_A^1. \end{aligned}$$

5.5 ***Basic reproduction number***

The basic reproduction number is denoted by R_0 and is defined as the expected number

of people getting secondary infection because of infected person enters into wholly susceptible population. This number determines the potential for the spread of disease within a population. When $R_0 < 1$ each infected individual produces on average less than one new infected individual so that the disease is expected to die out. On the other hand if $R_0 > 1$ then each individual produces more than one new infected individual so that the disease is expected to continue spreading in the population. This means that the threshold quantity for eradicating the disease is to reduce the value of R_0 to less than one.

The basic reproductive number R_0 can be determined using the next generation matrix. In this method R_0 is defined as the largest eigenvalue of the next generation matrix. The formulation of this matrix involves classification of all compartments of the model in to two classes: infected and non-infected.

Let f be a matrix of newly infected cases and v be a matrix of transition cases in model (1)-(10). Consider model (1)-(10)

$$
\begin{aligned}
dS/dt &= \tau - \frac{\beta_c BS}{\kappa + B} - \beta_h S I_h - \mu S \\
dI_c/dt &= \frac{\beta_c BS}{\kappa + B} - (\omega + \delta_1 + \mu) I_c \\
dR/dt &= \omega I_c - \mu R \\
dI_h/dt &= \beta_h S I_h - \frac{\beta_c B I_h}{\kappa + B} - (\gamma + \mu) I_h \\
dI_{hc}/dt &= \frac{\beta_c B I_h}{\kappa + B} - (\rho + \sigma + \delta_2 + \mu) I_{hc} \\
dA/dt &= \gamma I_h - \frac{\beta_c BA}{\kappa + B} - (\delta_3 + \mu) A \\
dA_c/dt &= \frac{\beta_c BA}{\kappa + B} + \rho I_{hc} - (\phi + \delta_4 + \mu) A_c \\
dR_h/dt &= \sigma I_{hc} - (\theta + \mu) R_h \\
dR_A/dt &= \theta R_h + \phi A_c - (\delta_5 + \mu) R_A \\
dB/dt &= \alpha B + \eta I_c - \nu B
\end{aligned}
$$

Now, f and v are given respectively as,

$$
f = \begin{bmatrix} \frac{\beta_c BS}{\kappa + B} \\ \beta_h S I_h \\ \frac{\beta_c B I_h}{\kappa + B} \\ \frac{\beta_c BA}{\kappa + B} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad v = \begin{bmatrix} (\omega + \delta_1 + \mu) I_c \\ \frac{\beta_c B I_h}{\kappa + B} + (\gamma + \mu) I_h \\ (\rho + \sigma + \delta_2 + \mu) I_{hc} \\ -\gamma I_h + \frac{\beta_c BA}{\kappa + B} + (\delta_3 + \mu) A \\ -\rho I_{hc} + (\phi + \delta_4 + \mu) A_c \\ -\sigma I_{hc} + (\theta + \mu) R_h \\ -\theta R_h - \phi A_c + (\delta_5 + \mu) R_A \\ -\alpha B - \eta I_c + \nu B \end{bmatrix},
$$

The Jacobian of f and v evaluated at disease free equilibrium point E_0 is given by F and V respectively as follows,

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & \beta_h S^0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} \omega + \delta_1 + \mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma + \mu & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho + \sigma + \delta_2 + \mu & 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & \delta_3 + \mu & 0 & 0 & 0 & 0 \\ 0 & 0 & -\rho & 0 & \phi + \delta_4 + \mu & 0 & 0 & 0 \\ 0 & 0 & -\sigma & 0 & 0 & \theta + \mu & 0 & 0 \\ 0 & 0 & 0 & 0 & -\phi & -\theta & \delta_5 + \mu & 0 \\ -\eta & 0 & 0 & 0 & 0 & 0 & 0 & \nu - \alpha \end{bmatrix}$$

The next generation matrix, FV^{-1} is computed and given by

$$FV^{-1} = \begin{bmatrix} \frac{\eta\beta_c S^0}{\kappa(\nu-\alpha)(\delta_1+\omega+\mu)} & 0 & 0 & 0 & 0 & 0 & \frac{\beta_c S^0}{\kappa(\nu-\alpha)} \\ 0 & \frac{\beta_h S^0}{\mu+\gamma} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

The eigenvalues of next generation matrix are computed and given by,

$$\lambda_1 = \frac{\eta\beta_c S^0}{\kappa(\nu-\alpha)(\delta_1+\omega+\mu)} = R_{0c}, \qquad \lambda_2 = \frac{\beta_h S^0}{\mu+\gamma} = R_{0h},$$

$$\lambda_3 = \lambda_4 = \lambda_5 = \lambda_6 = \lambda_7 = \lambda_8 = 0 \text{ with } \nu > \alpha.$$

Since reproduction number R_0 is the largest eigenvalue of next generation matrix, it is given by,

$$R_0 = max\{R_{0c}, R_{0h}\} \tag{32}$$

5.6 *Stability analysis of the disease free equilibrium point*

In the absence of the infectious disease, the model (1)-(10) have a unique disease free steady state E_0 . It is already shown that the DFE of model (1)-(10) is given by equation (31). The stability analysis of DFE is conducted and the results are presented in the form of theorems and proofs in the following sub-sections.

5.6.1 Local stability of disease free equilibrium point

Theorem 5.4 The DFE E_0 of the model (1)-(10) is locally asymptotically stable if $R_0 < 1$ and unstable otherwise.

Proof Consider the model (1)-(10) so that Jacobian matrix of the system at DFE is given by

$$J = \begin{bmatrix} -\mu & 0 & 0 & \beta_h S^0 & 0 & 0 & 0 & 0 & 0 & -\frac{\beta_c S^0}{\kappa} \\ 0 & -a & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & \omega & -\mu & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta_h S^0 - b & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -c & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \gamma & 0 & -d & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \rho & 0 & -e & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma & 0 & 0 & -f & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \phi & \theta & -g & 0 \\ 0 & \eta & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \alpha - \nu \end{bmatrix}$$

where $a = \omega + \delta_1 + \mu,\ b = \gamma + \mu,\ c = \rho + \sigma + \delta_2 + \mu,\ d = \delta_3 + \mu,\ e = \phi + \delta_4 + \mu,\ f = \theta + \mu,\ g = \delta_5 + \mu$. Now we compute the trace and determinant of Jacobian matrix to determine local stability of disease free equilibrium point. Simple mathematical computations gives the trace and determinant of the matrix as follows: Trace of $J < 0$ if $R_{0h} < 1$ and $\det(J) = \frac{bc\mu(R_{0h}-1)(defgu\alpha\kappa(\nu-a)(R_{0h}-1))}{\kappa} > 0$ if $R_{0h} < 1$ and $R_{0c} < 1$. Here, it can observed that, trace of a Jacobian matrix is less than zero and determinant of a matrix is greater than zero if $R_0 < 1$. Hence, by using trace-determinant principle we conclude that DFE is locally asymptotically stable if $R_0 < 1$.

6.5.2 Global stability of disease free equilibrium point

Let $x \in R^8$ is disease compartment and $y \in R^2$ be disease free compartment. The disease transmission model (1)-(10) can be written in the form:

$$\dot{x} = -(V - F)x - h(x, y)$$
$$\dot{y} = g(x, y)$$

where, $x = (I_c,\ I_h,\ I_{hc},\ A,\ A_c,\ R_h,\ R_A,\ B)$ and $y = (I_c,\ B)$. Further, the notations F and V are computed in subsection 5.5.

Theorem 5.5 If $V - F$ is a non-singular M-matrix and $h \geq 0$ then the disease-free equilibrium point of model (1)-(10) is globally asymptotically stable if $R_0 < 1$.

Proof The rate of change of the variables in the model equations (1)-(10) can be rewritten as

$$\dot{x} = -(V - F)x - \left[\left(\frac{\beta S_0}{\kappa} - \frac{\beta S}{\kappa + B}\right)\right]$$
$$\dot{S} = \tau - \frac{\beta_c B S}{\kappa + B} - \beta_h S I_h - \mu S$$
$$\dot{R} = \omega I_c - \mu R$$

where, F and V are computed and given by

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & \beta_h S^0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} a & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & c & 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & d & 0 & 0 & 0 & 0 \\ 0 & 0 & -\rho & 0 & e & 0 & 0 & 0 \\ 0 & 0 & -\sigma & 0 & 0 & f & 0 & 0 \\ 0 & 0 & 0 & 0 & -\phi & -\theta & g & 0 \\ -\eta & 0 & 0 & 0 & 0 & 0 & 0 & \nu - \alpha \end{bmatrix}.$$

Consider,

$$V - F = \begin{bmatrix} a & 0 & 0 & 0 & 0 & 0 & 0 & -\frac{\beta_c S^0}{\kappa} \\ 0 & b - \beta_h S^0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & c & 0 & 0 & 0 & 0 & 0 \\ 0 & -\gamma & 0 & d & 0 & 0 & 0 & 0 \\ 0 & 0 & -\rho & 0 & e & 0 & 0 & 0 \\ 0 & 0 & -\sigma & 0 & 0 & f & 0 & 0 \\ 0 & 0 & 0 & 0 & -\phi & -\theta & g & 0 \\ -\eta & 0 & 0 & 0 & 0 & 0 & 0 & \nu - \alpha \end{bmatrix} = sI - B,$$

where,

$$s = \max\{a, b, c, d, e, f, g, \nu - \alpha\},$$

and

$$B = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{\beta_c S^0}{\kappa} \\ 0 & \beta_h S^0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \phi & \theta & 0 & 0 \\ \eta & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}.$$

Thus, $V - F$ has Z sign pattern. Further, since $\det(V - F) = bcdefg\alpha(\nu - a)(R_{0h} - 1)(R_{0c} - 1) \neq 0$, it is clear that $V - F$ is non-singular matrix if $R_0 < 1$. Therefore, $V - F$ is non-singular M–matrix if $s > \rho(B) = max\left\{\beta_h S^0, \sqrt{\frac{\eta\beta_c S^0}{\kappa}}\right\}$. Next, we want show that $h(x, y) \geq 0$. Consider $h(x, y) = \left[\left(\frac{\beta S_0}{\kappa} - \frac{\beta S}{\kappa + B}\right)\right]$. At disease free equilibrium point, we observe that $S(t) \longrightarrow S_0$ as $t \longrightarrow \infty$. Hence, $h(x, y) \longrightarrow \mathbf{0}$ as

$$\begin{gathered}\big((S, \ I_c, \ R, \ I_h, \ I_{hc}, \ A, \ A_c, \ R_h, \ R_A, \ B)\big) \longrightarrow \\ (S_0, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0, \ 0 \ \ 0, \ 0).\end{gathered}$$

Therefore, from the above hypothesis the disease-free equilibrium point of model (1)-(10) is globally asymptotically stable for $R_0 < 1$.

5.6.3 Impact of HIV on Cholera infection

In order to express the impact of Cholera on HIV and impact of HIV on Cholera, we express R_{0c} interms R_{0h}. Since

$$R_{0h} = \frac{\beta_h \tau}{\mu(\mu+\gamma)} \Rightarrow \mu = \frac{\beta_h \tau}{R_{0h}(\mu+\gamma)}$$

Now, substituting the expression for μ in R_{0c} gives

$$R_{0c} = \frac{\eta\beta_c R_{0h}(\mu+\gamma)}{\beta_h \kappa(\nu-\alpha)(\delta_1+\omega+\mu)} .$$

To know the impact of diseases on each other we compute $\frac{\partial R_{0c}}{\partial R_{0h}}$ as

$$\frac{\partial R_{0c}}{\partial R_{0h}} = \frac{\eta\beta_c(\mu+\gamma)}{\beta_h \kappa(\nu-\alpha)(\delta_1+\omega+\mu)} > 0. \quad (33)$$

Equation (33) shows that increasing HIV cases increases Cholera cases and similarly increasing HIV cases increases Cholera cases.

6. Numerical simulation

In this section, numerical simulation study of model equations (1)-(10) is carried out using the software MATLAB. To conduct the study, a set of physically meaningful values are assigned to the model parameters. These values are either taken from literature or assumed on the basis of reality. These sets of parametric values are given under figures.

Figure 2 shows the change of human population with time. As it is seen on the figure 2 we observe the followings points (i) susceptible individuals decrease slowly as time increases whereas cholera only, HIV-Cholera only and AIDS-Cholera individuals decrease quickly with a significant number, due to impact of treatment, as time increases (ii) Recovered (R) individuals initially increase rapidly with a siginificant number and remain constant due to treatment impact as time increases (iii) HIV only, AIDS only, cholera recovered HIV only, and cholera recovered AIDS only individuals increase significantly. Moreover, the number of individuals with HIV only has a priority to AIDS only individuals to be recovered from cholera epidemics.

In Figure 3, we observe that the bacteria population decrease siginificantly over the first seven days and increase slowly as time increases.

7. Sensitivity analysis

Sensitivity analysis is used to determine the sensitivity of the model with respect to the parameters involved in it. That is, how changes in the value of the parameters of the model result in changing the dynamics of the infection. It is used to discover parameters that have a high impact on R_0 and should be targeted by intervention strategies. More precisely, sensitivity indices allow measuring the relative change in a variable when parameter changes. If the result is negative, then the relationship between the parameters and R_0 is inversely proportional. In this case, the modulus of the sensitivity index will be taken so that the size of the effect of changing that parameter can be deduced.

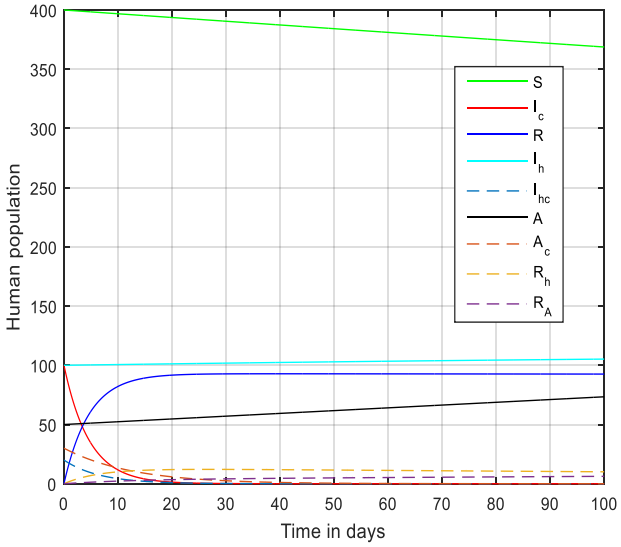

Figure 2. Simulations of human population variation with time with parameters value $\tau = \frac{0.045}{\text{day}}$, $\beta_c = \frac{0.01694}{\text{day}}$, $\beta_h = \frac{0.0000085}{\text{day}}$, $\omega = \frac{0.2}{\text{day}}$, $\gamma = \frac{0.0027}{\text{day}}$, $\rho = \frac{0.0085}{\text{day}}$, $\sigma = \frac{0.08}{\text{day}}$, $\phi = \frac{0.01}{\text{day}}$, $\theta = \frac{0.0027}{\text{day}}$, $\delta_1 = \frac{0.015}{\text{day}}$, $\delta_2 = \frac{0.045}{\text{day}}$, $\delta_3 = \frac{0.00065}{\text{day}}$, $\delta_4 = \frac{0.075}{\text{day}}$, $\delta_5 = \frac{0.00065}{\text{day}}$, $\mu = \frac{0.000048}{\text{day}}$, $\kappa = 107\left(\frac{\text{cell}}{\text{ml}}\right)$, $\nu = \frac{1.06}{\text{day}}$, $\eta = 10$ (cell/ml /day / person), $\alpha = 0.073/\text{day}$.

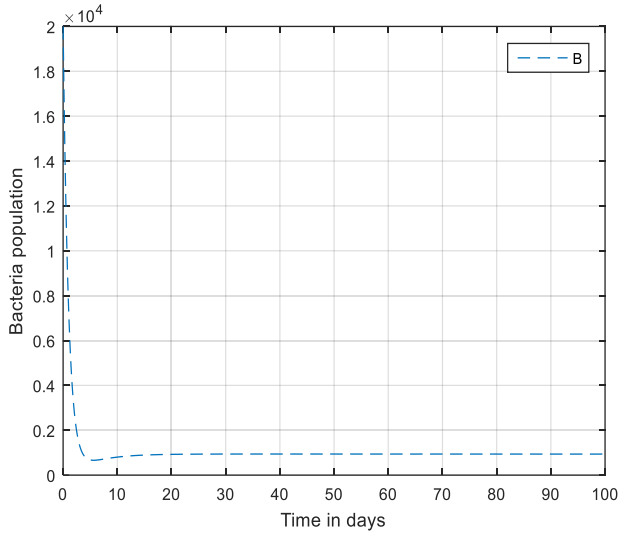

Figure 3. Simulation of bactreria population variation with time. with parameters value $\tau = \frac{0.045}{\text{day}}$, $\beta_c = \frac{0.01694}{\text{day}}$, $\beta_h = \frac{0.0000085}{\text{day}}$, $\omega = \frac{0.2}{\text{day}}$, $\gamma = \frac{0.0027}{\text{day}}$, $\rho = \frac{0.0085}{\text{day}}$, $\sigma = \frac{0.08}{\text{day}}$, $\phi = \frac{0.01}{\text{day}}$, $\theta = \frac{0.0027}{\text{day}}$, $\delta_1 = \frac{0.015}{\text{day}}$, $\delta_2 = \frac{0.045}{\text{day}}$, $\delta_3 = \frac{0.00065}{\text{day}}$, $\delta_4 = \frac{0.075}{\text{day}}$, $\delta_5 = \frac{0.00065}{\text{day}}$, $\mu = \frac{0.000048}{\text{day}}$, $\kappa = 107\left(\frac{\text{cell}}{\text{ml}}\right)$, $\nu = \frac{1.06}{\text{day}}$, $\eta = 10$ (cell/ml /day / person), $\alpha = 0.073/\text{day}$.

On the other hand, a positive sensitivity index means that both the function and the parameter are proportional to each other i.e. both of them grow or decay together.

It is already shown that the explicit expression of R_0 is given by $R_0 = \frac{\beta_h \tau}{\mu(\mu+\gamma)}$. Since, R_0 depends only on four parameters, an analytical expression will be derived for its sensitivity to each of the parameters using the normalized forward sensitivity index as given by Chitnis [3].

$$\Upsilon_{\beta_h}^{R_0} = [\partial R_0/\partial \beta_h] \times [\beta_h/R_0]$$
$$\Upsilon_{\tau}^{R_0} = [\partial R_0/\partial \tau] \times [\tau/R_0]$$
$$\Upsilon_{\gamma}^{R_0} = [\partial R_0/\partial \gamma] \times [\gamma/R_0]$$
$$\Upsilon_{\mu}^{R_0} = [\partial R_0/\partial \mu] \times [\mu/R_0]$$

Table 1. Sensitivity of R_0 evaluated for the parametric values.

Parameter	Sensitivity index
β_h	+1
τ	+1
γ	-
μ	-

As it is described in Table 1, parameters τ and β_h have a positive sensitivity indices and other two parameters γ and μ have negative sensitivity indices. Hence, increasing a value of a parameter with positive sensitivity indices will cause an increasing R_0 which implies that disease spread in population. Similarly, increasing a value of a parameter with negative sensitivity indices will cause an decrease R_0 which implies that disease in population extinct or can be controlled using the the available controlling mechanism.

8. Result and discussion

In this study, a model of HIV and Cholera coinfection is formulated. We have observed that, the transmission and recruitment rates have a positive impact on co-dynamics of infections whereas natural death rate and recovery rate have negative impact on the transmisions of the infections. The result of stability analysis shows that if the reproduction number $R_0 < 1$, the infection free equilibrium point is both locally and globally asymptotically stable, otherwise unstable. The numerical simulations shows that an effective usage of medical treatments and necessary measures, toward cholera, can siginificantly support to totally control the epidemic or reduce the number of infectious individuals. Figure 2 shows that in the presence of treatments Cholera infected individuals can be recovered and the infection can also be controlled. On the other hand, HIV/AIDS infections can be controlled using ART or HAART that siginificantly reduces the number of viral loads in the body and elongates life of patients. Figure 3 shows that the presence of toxic bacterium in the environment can be reduced at the beginning by using necessary measures such as sanitation and treatments. Further, taking cares for HIV/AIDS patients reduces the chance to be easily attacked from the environment that contaminated with toxic bacterium that causes cholera infections.

9. Conclusion

In this study, a new ten compartmental model of HIV-Cholera coinfection is developed and the stability of equilibrium points are analyzed. The formulated model is well-posed. It is also observed that, HIV has a positive impact on Cholera and Cholera has a positive impact on Cholera. Effective treatment helps in making population free of Cholera infection and controlling HIV infection.

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