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Mathematical Model for Transmission Dynamics of Hepatitus C Virus with Optimal Control Strategies

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Abstract. An epidemic model with optimal control strategies was investigated for Hepatitus C Viral disease that can be transmitted through infected individuals. In this study, we used a deterministic compartmental model for assessing the effect of different optimal control strategies for controlling the spread of Hepatitus C disease in the community. Stability theory of differential equations is used to study the qualitative behavior of the system. The basic reproduction number that represents the epidemic indicator is obtained by using the condition of endemicity. Both the local stability and global stability conditions for disease free equilibrium is established. Uniqueness of endemic equilibrium point and its global stability conditions are proved. Numerical simulation of the model showed that applying all the intervention strategies can successfully eliminate Hepatitus C viral disease from the community.

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1. Introduction

Hepatitis (plural hepatitides) is an inflammation of the liver characterized by the presence of inflammatory cells in the tissue of the organ [18]. The inflammation of liver causes soreness and swelling. Hepatitis is most commonly caused by one of the 5 hepatitis viruses; hepatitis A, hepatitis B, hepatitis C, hepatitis D and hepatitis E. Hepatitis C is usually spread through contact with blood products [11]. Blood products have been the main agents through which HCV is transmitted, but ever since 1992, when it became possible to detect the virus in blood, transmissions through transfusions, and organ transmissions have been minimal. Most common avenues through which HCV is spread are unprotected sex, sharing of contaminated needles among drug addicts and those with other STDs [19]. Some people also get this virus from tattoo and piercing salons. It is also possible to contract HCV at birth, as it can be transmitted from mother to baby.

Hepatitis C is very common, potentially fatal disease. Globally, an estimated 170 million people are living with HCV [10]. This infection is very common in developing countries. In Egypt, prevalence ranges from 18-35% in different parts. Even in some developed countries like Australia, an estimated 200,000 people are living with HCV,

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with approximately 150,000 having chronic HCV infection [6] (Figure 1).

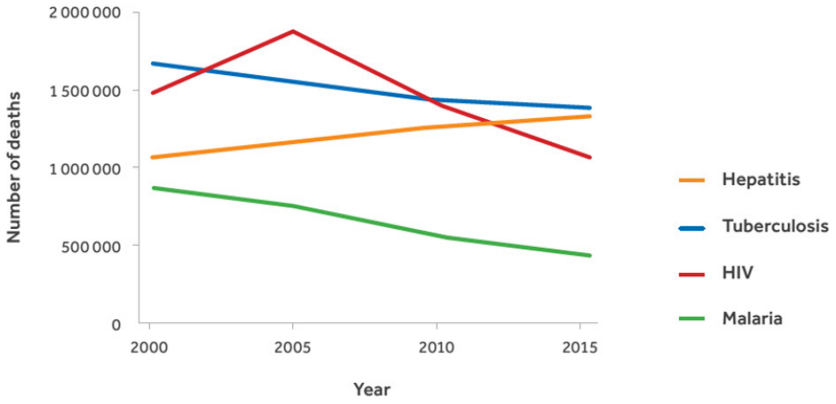

Figure 1. Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000-2015.

HCV is undoubtedly the most important cause of chronic Hepatitis. It has also been reported to be associated with acute hepatitis, autoimmune chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma [16]. Because the infection becomes chronic in more than 80% of in the infected people, the disease is an important public health and economic problem [3].

Different mathematical models have been developed to analyze the transmission dynamics of HCV as well as the effectiveness of some intervention strategies against the spread of HCV infections. For example, Martcheva and Castillo-Chavez considered a model of HCV with chronic infectious stage in a varying population [9]. Their model was extended by Yuan and Yang to include the latent period [20]. In particular, there have been studies of epidemiological models where optimal control methods were applied. These include Kazeem Oare Okosun [14] who studied SEITV (Susceptible, Exposed, Infected, Treated and Vaccinated) epidemic model and applied stability analysis theory to find the equilibrium solutions and then used optimal control to determine the optimal vaccination strategies to reduce acute and chronic stages in the presence of treatment and infected immigrants. A similar study conduct was also conducted by Neterindwa Ainea et al. without using optimal control strategies [1]. All of the above studies reveal an important result for HCV disease transmission dynamics by considering different conditions. In this study, we will consider a *PSIcIR* (Protection, Susceptible, Carrier, Infected, and Recovered) model for HCV. Our model is a modified and extended version of the model presented in [13] with optimal control strategies for the control of the disease.

2. Description and formulation of model

The compartments used in this model consist of five classes: $P(t)$ is the compartment used for those which are protected against the disease over a period of time. $S(t)$ is used to represent the number of individuals that are prone to the disease at time *t.* $I(t)$ denotes the number of individuals who have been infected with the disease and are capable of spreading the disease to those in the susceptible categories. $I_c(t)$ denotes the number of individuals who are infected with the disease and are capable of spreading the disease without showing any symptoms of the disease. $R(t)$ denote the number of individuals who are recovered from the disease. Protected individuals are recruited into the population

at per capita rate $(1-\alpha)\Lambda$. Susceptible individuals are recruited into the population at per capita rate $\alpha\Lambda$. Susceptible individuals acquire typhoid infection at per capita rate λ. The susceptible class is increased by birth or emigration at a rate of $\alpha\Lambda$ and also from recovered class by losing temporary immunity with δ rate and from protected class by losing protection with γ rate. λ is the effective force of infection which is given by $\lambda = (\beta_1 A + \beta_2 C)/N$ where β_1 is effective contact rate of individuals with acute HCV infected and β_2 is effective contact rate of individuals with chronic HCV infected. φ is the rate at which acute infected individuals become chronically infected. μ is the natural mortality rate, d_1 is the disease induced mortality rate due to acute infection, d_2 is the disease induced mortality rate due to chronic infection. β is the rate of treatment of chronically infected and joining recovered class, θ is the rate of treatment of acute infected and joining recovered class.

The acute infected subclass is increased from susceptible subclass by $\rho\lambda$ screening rate. The chronic infected subclass is increased from susceptible subclass by $(1-\rho)\lambda$ screening rate. Those individuals in the acute infected subclass can get treatment and join recovered subclass with a rate of θ. And those individuals in the chronic infected subclass can get treatment and join recovered subclass with a rate of β. The recovered subclass also increases with individuals who come from acute infected class by getting treatment with a rate of θ and chronic infected class by getting treatment with a rate of β. In all the subclasses, μ is the natural death rate of individuals, but in the acute infective class d_1 is disease induced death rate due to acute infection and d_2 is the disease induced death rate due to chronic infection. The assumption of this model is that there is re-infection once an individual is recovered (Figure 2).

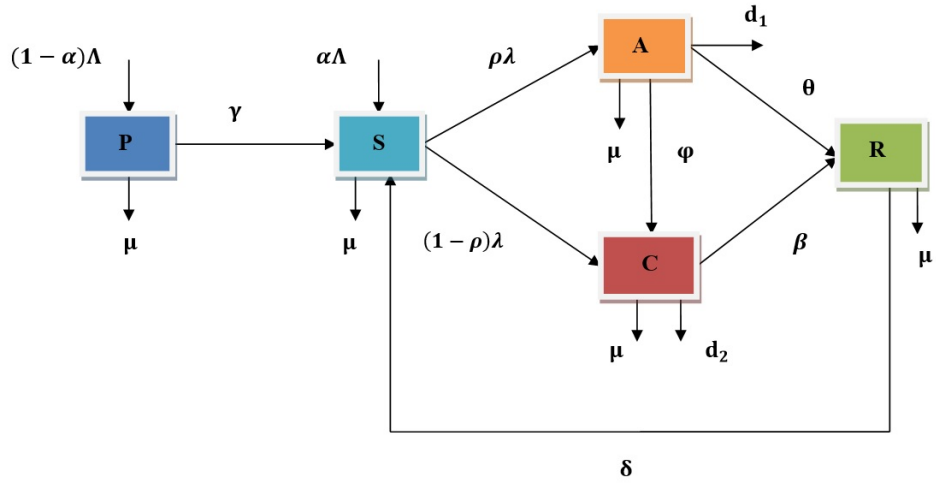

Figure 2. Flow diagram of the model.

The above model description can be written in five system of differential equation below.

$$\frac{dP}{dt} = (1-\alpha)\Lambda - (\gamma + \mu)P, \tag{1}$$

$$\frac{dS}{dt} = \alpha\Lambda + \gamma P + \delta R - (\lambda + \mu)S, \tag{2}$$

$$\frac{dA}{dt} = \rho\lambda S - (\varphi + \theta + d_1 + \mu)A, \tag{3}$$

$$\frac{dC}{dt} = (1-\rho)\lambda S + \varphi A - (\beta + d_2 + \mu)C, \tag{4}$$

$$\frac{dR}{dt} = \theta A + \beta C - (\mu + \delta)R, \tag{5}$$

where $\lambda = (\beta_1 A + \beta_2 C)/N$ is effective force of infection, β_1 is effective contact rate of individuals with acute HCV infected and β_2 is effective contact rate of individuals with chronic HCV infected. Shortly we may write $\lambda = \varepsilon_1 A + \varepsilon_2 C$ for the sake of simplicity, where $\varepsilon_1 = \frac{\beta_1}{N}$ and $\varepsilon_2 = \frac{\beta_2}{N}$ then $\lambda = \varepsilon_1 A + \varepsilon_2 C$, $N = P + S + A + C + R$ with initial conditions $P(0) = P_0$, $S(0) = S_0$, $A(0) = A_0$, $C(0) = C_0$, $R(0) = R_0$.

3. The model analysis

We assumed the initial condition of the model is non-negative, and now we will show that the solution of the model is also positive.

3.1. *Positivity of Solution*

Theorem 3.1 Let $\Omega = \left\{(P,S,A,C,R) \in R_+^5 : P_0 > 0, S_0 > 0, A_0 > 0, C_0 > 0, R_0 > 0\right\}$ then the solutions $\{P,S,A,C,R\}$ are positive for $t \geq 0$.

Proof From the system of differential equation, taking the first equation

$$\frac{dP}{dt} = (1-\alpha)\Lambda - (\gamma + \mu)P$$

$$\Rightarrow \frac{dP}{dt} \geq -(\gamma + \mu)P \qquad \text{(because } (1-\alpha)\Lambda \geq 0)$$

$$\Rightarrow \frac{dP}{P} \geq -(\gamma + \mu)dt$$

$$\Rightarrow \int \frac{dP}{P} \geq -\int (\gamma + \mu)\, dt$$

$$\Rightarrow \ln P \geq -(\gamma + \mu)t + C_1 \qquad \text{where } C_1 \text{ is integration constant}$$

$$\Rightarrow P(t) \geq P_0 e^{-(\gamma+\mu)t} \qquad \text{where } P(0) = P_0 = C_1$$

$$\therefore \ P(t) \geq 0 \quad \text{for all } t \geq 0.$$

From the second equation, we have

$$\frac{dS}{dt} = \alpha\Lambda + \gamma P + \delta R - (\lambda + \mu)S$$

$$\Rightarrow \frac{dS}{dt} \geq \delta R - (\lambda + \mu)S$$

$$\Rightarrow \frac{dS}{dt} + (\lambda + \mu)S \geq \delta R$$

Using appropriate integrating factor $e^{\int (\lambda+\omega)\, dt}$ and re-arranging we get

$$S(t) \geq \frac{\Lambda}{\alpha\mu} + \left(S_0 - \frac{\Lambda}{\alpha\mu} \right) e^{-(\lambda+\mu)t}$$

$$\Rightarrow \liminf_{t\to\infty} S(t) \geq 0$$

$$\therefore \quad S(t) \geq 0 \quad \text{for all} \quad t \geq 0.$$

From the third equation, we have

$$\frac{dA}{dt} = \rho\lambda S - (\varphi + \theta + d_1 + \mu) A$$

$$\Rightarrow \frac{dA}{dt} \geq -(\varphi + \theta + d_1 + \mu) A$$

$$\Rightarrow \frac{dA}{A} \geq -(\varphi + \theta + d_1 + \mu) dt$$

$$\Rightarrow \int \frac{dA}{A} \geq -\int (\varphi + \theta + d_1 + \mu)\ dt$$

$$\Rightarrow \ln A \geq -(\varphi + \theta + d_1 + \mu)t + C_2 \quad \text{where } C_2 \text{ is integration constant}$$

$$\Rightarrow A(t) \geq A_0 e^{-(\varphi+\theta+d_1+\mu)t} \quad \text{where } A_0 = A(0) = C_2$$

$$\therefore \quad A(t) \geq 0 \quad \text{for all} \quad t \geq 0.$$

From the fourth equation, we have

$$\frac{dC}{dt} = (1-\rho)\lambda S + \varphi A - (\beta + \mathrm{d}_2 + \mu)\mathrm{C}$$

$$\Rightarrow \frac{dC}{dt} \geq -(\beta + d_2 + \mu) C$$

$$\Rightarrow \frac{dC}{c} \geq -(\beta + d_2 + \mu) dt$$

$$\Rightarrow \int \frac{dC}{C} \geq -\int (\beta + d_2 + \mu)\ dt$$

$$\Rightarrow \ln C \geq -(\beta + d_2 + \mu)t + C_3 \quad \text{where } C_3 \text{ is integration constant}$$

$$\Rightarrow C(t) \geq C_0 e^{-(\beta+d_2+\mu)t} \quad \text{where } C_0 = C(0) = C_3$$

$$\therefore \quad C(t) \geq 0 \quad \text{for all} \quad t \geq 0.$$

From the fifth equation, we have

$$\frac{dR}{dt} = \theta A + \beta C - (\mu + \delta)\mathrm{R}$$

$$\Rightarrow \frac{dR}{dt} \geq -(\mu + \delta)\mathrm{R}$$

$$\Rightarrow \frac{dR}{R} \geq -(\mu + \delta) dt$$

$$\Rightarrow \int \frac{dR}{R} \geq -\int (\mu + \delta)\ dt$$

$$\Rightarrow \ln R \geq -(\mu + \delta)t + C_4 \quad \text{where } C_4 \text{ is integration constant}$$

$$\Rightarrow R(t) \geq R_0 e^{-(\mu+\delta)t} \quad \text{where } R_0 = R(0) = C_3$$

$$\therefore \quad R(t) \geq 0 \quad \text{for all} \quad t \geq 0.$$

This completes the proof of the theorem. ■

Therefore, the solution of the model is positive.

3.2. *Invariant region*

Theorem 3.2 The total population size N of the system of model equations (1)-(5) is bounded in the invariant region Ω. That is, size of $N(t)$ is bounded for all t.

Proof In the given model the total population (N) is

$$N = P + S + A + C + R.$$

Based on the techniques on [4] we differentiating N both sides with respect to t leads to

$$\frac{dN}{dt} = \frac{dP}{dt} + \frac{dS}{dt} + \frac{dA}{dt} + \frac{dC}{dt} + \frac{dR}{dt}. \tag{6}$$

By substituting (1)-(5) into (6), we can get

$$\frac{dN}{dt} = \Lambda - \mu N - \left(d_1 A + d_2 C\right). \tag{7}$$

In the absence of mortality due to typhoid disease (i.e, $d_1 = d_2 = 0$), equation (7) becomes

$$\frac{dN}{dt} \le \Lambda - \mu N, \tag{8}$$

Rearranging and integrating both sides of (8), we get

$$\int \frac{dN}{\Lambda - \mu N} \le \int dt$$

$$\Rightarrow \frac{-1}{\mu} \ln(\Lambda - \mu N) \le t + C_5 \quad \text{where } C_5 \text{ is integration constant}$$

$$\Rightarrow \ln(\Lambda - \mu N) \ge -\mu t + C_6 \quad \text{where } C_6 = -\mu C_5$$

$$\Rightarrow \Lambda - \mu N \ge A e^{-\mu t} \quad \text{where } A = e^{C_6}$$

By applying initial condition $N(0) = N_0$, we get

$$A = \Lambda - \mu N_0$$

$$\Rightarrow \Lambda - \mu N \ge \left(\Lambda - \mu N_0\right) e^{-\mu t}$$

$$\Rightarrow N \le \frac{\Lambda}{\mu} - \left[\frac{\Lambda - \mu N_0}{\mu}\right] e^{-\mu t} \tag{9}$$

As $t \to \infty$ in (9), the population size $N \to \frac{\Lambda}{\mu}$ which implies that $0 \le N \le \frac{\Lambda}{\mu}$. Thus, the feasible solution set of the model enters and remain in the region:

$$\Omega = \left\{(P, S, A, C, R) \in R_+^5 : \mathrm{N} \le \tfrac{\Lambda}{\mu}\right\}.$$

Therefore, the basic model is well posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of the basic model in Ω .

Lemma 3.1 (Existence of solution) Solutions of the model equations (1)-(5) together with the initial conditions $P(0) > 0$, $S(0) > 0$, $A(0) > 0$, $C(0) > 0$, $R(0) > 0$ exist in $\mathbb{R}_+^5$, i.e., the solution of the model $P(t)$, $S(t)$, $A(t)$, $C(t)$ and $R(t)$ exist for all t and will remain in $\mathbb{R}_+^5$.

Proof The right hand sides of the system of equations (1)-(5) can be expressed as follows:

$$f_1(P, S, A, C, R) = (1 - \alpha)\Lambda - (\gamma + \mu)P,$$

$$f_2(P,S,A,C,R) = \alpha\Lambda + \gamma P + \delta R - (\lambda + \mu)S,$$
$$f_3(P,S,A,C,R) = \rho\lambda S - (\varphi + \theta + d_1 + \mu)A,$$
$$f_4(P,S,A,C,R) = (1-\rho)\lambda S + \varphi A - (\beta + d_2 + \mu)C,$$
$$f_5(P,S,A,C,R) = \theta A + \beta C - (\mu + \delta)R.$$

According to Derrick and Grobsman theorem, let Ω denote the region

$$\Omega = \left\{(P,S,A,C,R) \in \mathbb{R}_+^5 : N \le (\Lambda / \mu)\right\}.$$

Then equations (1)-(5) have a unique solution if $(\partial f_i)/(\partial x_j)$, $i, j = 1,2,3,4,5$ are continuous and bounded in Ω. Here, $x_1 = P$, $x_2 = S$, $x_3 = A$, $x_4 = C$ and $x_5 = R$.

For f_1 :

$$\left|(\partial f_1)/(\partial P)\right| = \left|-(\gamma + \mu)\right| < \infty,$$
$$\left|(\partial f_1)/(\partial S)\right| = 0 < \infty,$$
$$\left|(\partial f_1)/(\partial A)\right| = 0 < \infty,$$
$$\left|(\partial f_1)/(\partial C)\right| = 0 < \infty,$$
$$\left|(\partial f_1)/(\partial R)\right| = 0 < \infty.$$

For f_2 :

$$\left|(\partial f_2)/(\partial P)\right| = \left|\gamma\right| < \infty,$$
$$\left|(\partial f_2)/(\partial S)\right| = \left|-(\lambda + \mu)\right| < \infty,$$
$$\left|(\partial f_2)/(\partial A)\right| = 0 < \infty,$$
$$\left|(\partial f_2)/(\partial C)\right| = 0 < \infty,$$
$$\left|(\partial f_2)/(\partial R)\right| = \left|\delta\right| < \infty.$$

For f_3 :

$$\left|(\partial f_3)/(\partial P)\right| = 0 < \infty,$$
$$\left|(\partial f_3)/(\partial S)\right| = \left|\rho\lambda\right| < \infty,$$
$$\left|(\partial f_3)/(\partial A)\right| = \left|-(\varphi + \theta + d_1 + \mu)\right| < \infty,$$
$$\left|(\partial f_3)/(\partial C)\right| = 0 < \infty,$$
$$\left|(\partial f_3)/(\partial R)\right| = 0 < \infty.$$

For f_4 :

$$\left|(\partial f_4)/(\partial P)\right| = 0 < \infty,$$
$$\left|(\partial f_4)/(\partial S)\right| = \left|(1-\rho)\lambda\right| < \infty,$$
$$\left|(\partial f_4)/(\partial A)\right| = \left|\varphi\right| < \infty,$$
$$\left|(\partial f_4)/(\partial C)\right| = \left|-(\beta + d_2 + \mu)\right| < \infty,$$
$$\left|(\partial f_4)/(\partial R)\right| = 0 < \infty.$$

For f_5 :

$$\left|\left(\partial f_5\right)/(\partial P)\right| = 0 < \infty,$$
$$\left|\left(\partial f_5\right)/(\partial S)\right| = 0 < \infty,$$
$$\left|\left(\partial f_5\right)/(\partial A)\right| = \left|\theta\right| < \infty,$$
$$\left|\left(\partial f_5\right)/(\partial C)\right| = \left|\beta\right| < \infty,$$
$$\left|\left(\partial f_5\right)/(\partial R)\right| = \left|-(\mu+\delta)\right| < \infty.$$

Thus, all the partial derivatives $\left(\partial f_i\right)/\left(\partial x_j\right),\ i, j = 1,2,3,4$ exist, continuous and bounded in Ω. Hence, by Derrick and Grobsman theorem, a solution for the model (1)-(5) exists and is unique. ■

3.3. *Disease free equilibrium (DFE)*

To find the disease free equilibrium we consider the steady state of the system (1)-(5) which is

$$\begin{aligned}
&(1-\alpha)\Lambda - (\gamma+\mu)P = 0,\\
&\alpha\Lambda + \gamma P + \delta R - (\lambda+\mu)S = 0,\\
&\rho\lambda S - \left(\varphi+\theta+d_1+\mu\right)A = 0,\\
&(1-\rho)\lambda S + \varphi A - \left(\beta+d_2+\mu\right)C = 0,\\
&\theta A + \beta C - (\mu+\delta)R = 0.
\end{aligned} \tag{10}$$

Equating (10) at $A = 0,\ C = 0$ and solving the non-infected state variables. We get the following

From the first equation of (10), $(1-\alpha)\Lambda - (\gamma+\mu)P = 0$. Solving for P we get

$$P = \frac{(1-\alpha)\Lambda}{\gamma+\mu}.$$

From the second equation of (10), $\alpha\Lambda + \gamma P + \delta R - (\lambda+\mu)S = 0$. Solving for S we get

$$S = \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)}.$$

Therefore, the disease free equilibrium E_0 becomes

$$E_0 = \left(\frac{(1-\alpha)\Lambda}{\gamma+\mu},\ \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)}, 0, 0, 0\right).$$

3.4. *Endemic equilibrium point*

To find the endemic equilibrium point E^* we considered the steady state of the system (1)-(5) for all state variables.

From the first equation of (10) we have

$$(1-\alpha)\Lambda - (\gamma+\mu)P^* = 0$$
$$\Rightarrow P^* = \frac{(1-\alpha)\Lambda}{\gamma+\mu}$$

Let

$$y = \varepsilon_1 A + \varepsilon_2 C. \tag{11}$$

From the third equation of (10) we have

$$\rho\lambda S^* - (\varphi + \theta + d_1 + \mu)A^* = 0$$
$$\Rightarrow \rho y S^* = (\varphi + \theta + d_1 + \mu)A^*$$
$$\Rightarrow y = \frac{(\varphi + \theta + d_1 + \mu)A^*}{\rho S^*} \tag{12}$$

From the fourth of (10) equation we have

$$(1-\rho)\lambda S^* + \varphi A^* - (\beta + d_2 + \mu)C^* = 0$$
$$\Rightarrow (1-\rho) y S^* + \varphi A^* - (\beta + d_2 + \mu)C^* = 0$$

Substituting equation (12) here we get

$$(1-\rho)\frac{(\varphi + \theta + d_1 + \mu)A^*}{\rho S^*} S^* + \varphi A^* - (\beta + d_2 + \mu)C^* = 0$$
$$\Rightarrow (1-\rho)(\varphi + \theta + d_1 + \mu)A^* + \rho\varphi A^* - (\beta + d_2 + \mu)\rho C^* = 0$$
$$\Rightarrow \left[(1-\rho)(\varphi + \theta + d_1 + \mu) + \rho\varphi\right]A^* = (\beta + d_2 + \mu)\rho C^*$$
$$\Rightarrow \quad C^* = \frac{\left[(1-\rho)(\varphi + \theta + d_1 + \mu) + \rho\varphi\right]A^*}{\rho(\beta + d_2 + \mu)} \tag{13}$$

From the fifth equation of (10) we have

$$\theta A^* + \beta C^* - (\mu + \delta)R^* = 0$$
$$\Rightarrow R^* = \frac{\theta A^* + \beta C^*}{\mu + \delta} \tag{14}$$

Substituting equation (13) into (14) we get

$$R^* = \frac{\theta A^* + \beta \dfrac{\left[(1-\rho)(\varphi + \theta + d_1 + \mu) + \rho\varphi\right]A^*}{\rho(B + d_2 + \mu)}}{\mu + \delta}$$
$$\Rightarrow R^* = \frac{A^*\rho\theta(\beta + d_2 + \mu) + \beta(\varphi + \theta + d_1 + \mu) - \rho\beta(\theta + d_1 + \mu)}{\rho(\mu + \delta)(\beta + d_2 + \mu)} \tag{15}$$

Now from equation (12) we have

$$y = \frac{(\varphi + \theta + d_1 + \mu)A^*}{\rho S^*}$$
$$\Rightarrow S^* = \frac{(\varphi + \theta + d_1 + \mu)A^*}{\rho y} \tag{16}$$

From equation (11), $y = \varepsilon_1 A + \varepsilon_2 C$ and using equation (13) we get

$$y = \varepsilon_1 A + \varepsilon_2 \frac{\left[(1-\rho)(\varphi + \theta + d_1 + \mu) + \rho\varphi\right]A^*}{\rho(\beta + d_2 + \mu)}, \tag{17}$$

Substituting equation (17) in (16) we get

$$S^* = \frac{(\varphi + \theta + d_1 + \mu)A^*}{\rho\left[\varepsilon_1 A^* + \varepsilon_2 \dfrac{\left[(1-\rho)(\varphi + \theta + d_1 + \mu) + \rho\varphi\right]A^*}{\rho(\beta + \Delta_2 + \mu)}\right]}$$

$$\Rightarrow S^* = \frac{(\varphi+\theta+\Delta_1+\mu)}{\rho\left(\varepsilon_1+\varepsilon_2\dfrac{\left[(1-\rho)(\varphi+\theta+\Delta_1+\mu)+\rho\varphi\right]}{\rho(\beta+\Delta_2+\mu)}\right)}$$

$$\Rightarrow S^* = \frac{\rho(\varphi+\theta+d_1+\mu)(\beta+d_2+\mu)}{\rho(\rho\varepsilon_1+\varepsilon_2(1-\rho)(\varphi+\theta+d_1+\mu)+\varepsilon_2\rho\varphi)}$$

$$\Rightarrow S^* = \frac{(\varphi+\theta+d_1+\mu)(\beta+d_2+\mu)}{(\rho\varepsilon_1+\varepsilon_2(1-\rho)(\varphi+\theta+d_1+\mu)+\varepsilon_2\rho\varphi)} \tag{18}$$

Again, we consider equation (15). For the sake of simplicity put

$$a = \frac{\left[\rho\theta(\beta+d_2+\mu)+\beta(\varphi+\theta+d_1+\mu)-\rho\beta(\theta+d_2+\mu)\right]}{\rho(\mu+\delta)(\beta+d_2+\mu)}.$$

Thus equation (15) can be shortly written as

$$R^* = aA^*. \tag{19}$$

Now taking the second equation of the steady state (10)

$$\alpha\Lambda+\gamma P^*+\delta R^*-(\lambda+\mu)S^* = 0$$

$$\Rightarrow \alpha\Lambda+\gamma P^*+\delta R^*-\left(\varepsilon_1 A^*+\varepsilon_2 C^*\right)S^*-\mu S^* = 0 \tag{20}$$

From equation (13) we have

$$C^* = bA^*. \tag{21}$$

where $b = \left[(1-\rho)(\varphi+\theta+d_1+\mu)+\rho\varphi\right]/\rho(\beta+d_2+\mu).$

Substituting equation (19) and (21) into equation (20) we get

$$\alpha\Lambda+\gamma P^*+\delta aA^*-\left(\varepsilon_1 A^*+\varepsilon_2 bA^*\right)S^*-\mu S^* = 0$$

$$\Rightarrow A^*\left[\delta a-(\varepsilon_1+\varepsilon_2 b)S^*\right] = \mu S^*-\alpha\Lambda-\gamma P^*$$

$$\Rightarrow A^* = \frac{\mu S^*-\alpha\Lambda-\gamma P^*}{\delta a-(\varepsilon_1+\varepsilon_2 b)S^*} \tag{22}$$

From equation (21) we have

$$C^* = \frac{\left[(1-\rho)(\varphi+\theta+d_1+\mu)+\rho\varphi\right]}{\rho(\beta+d_2+\mu)}\left(\frac{\mu S^*-\alpha\Lambda-\gamma P^*}{\delta a-(\varepsilon_1+\varepsilon_2 b)S^*}\right).$$

From equation (19) we have

$$R^* = \frac{\left[\rho\theta(\beta+d_2+\mu)+\beta(\varphi+\theta+d_1+\mu)-\rho\beta(\theta+d_1+\mu)\right]}{\rho(\mu+\delta)(\beta+d_2+\mu)}\left(\frac{\mu S^*-\alpha\Lambda-\gamma P^*}{\delta a-(\varepsilon_1+\varepsilon_2 b)S^*}\right).$$

Therefore, $E^* = \left(P^*, S^*, A^*, C^*, R^*\right)$ is an endemic equilibrium point such that $P^* > 0$, $S^* > 0$, $A^* > 0$, $C^* > 0$, $R^* > 0$ exists.

3.5. *Basic reproduction number* $(\Re_0)$

The basic reproduction number is the average number of secondary cases a typical infectious individual will cause in a completely susceptible population [2]. In this section, we obtained the basic reproduction number which is the threshold parameter that governs the spread of the disease. For the given model the endemic equilibrium point E^* exists in the feasible region D, the necessary and sufficient condition is that:

$$0 < S^* < \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)} \text{ or equivalently } \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)S^*} \geq 1.$$

Define $\Re_0 = \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)S^*}$, thus

$$\Re_0 = \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)} \frac{\left[\rho\varepsilon_1(\beta+d_2+\mu)+\varepsilon_2(1-\rho)(\varphi+\theta+d_1+\mu)+\varepsilon_2\rho\varphi\right]}{(\varphi+\theta+d_1+\mu)(\beta+d_2+\mu)},$$

$$\therefore \Re_0 = \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)}\left[\frac{\rho\varepsilon_1}{(\varphi+\theta+d_1+\mu)} + \frac{\varepsilon_2(1-\rho)}{(\beta+d_2+\mu)} + \frac{\varepsilon_2\rho\varphi}{(\varphi+\theta+d_1+\mu)(\beta+d_2+\mu)}\right]. \quad (23)$$

Since $\varepsilon_1 = \frac{\beta_1}{N}$ and $\varepsilon_2 = \frac{\beta_2}{N}$ the basic reproduction number on (23) becomes

$$\therefore \Re_0 = \frac{(r+\alpha\mu)}{(\mu+\gamma)}\left[\frac{\rho\beta_1}{(\varphi+\theta+d_1+\mu)} + \frac{\beta_2(1-\rho)}{(\beta+d_2+\mu)} + \frac{\beta_2\rho\varphi}{(\varphi+\theta+d_1+\mu)(\beta+d_2+\mu)}\right].$$

Considering equation (23) above, we give interpretation of the basic reproduction number for our model as follows.

When a single infective is introduced in a population with a probability ρ it is acute infected, it makes β_1 contact per unit time. This is multiplied by the average infectious period $1/(\varphi+\theta+d_1+\mu)$ for acute infectious; with probability $1-\rho$ the infective is a chronic, and hence make β_2 effective per unit time during the average time $1/(\beta+d_2+\mu)$ it remains a chronic infected. This number should be augmented by the number of infectious $\rho\beta_2/(\beta+d_2+\mu)$ caused by this infective after it becomes acute infectious, with a probability $\varphi/(\varphi+\theta+d_1+\mu)$ to survive the acute stage. Therefore, the expression in the square bracket in (23) is the per capita average number of secondary infections. This number multiplied by the number of susceptible at disease free equilibrium, $\Lambda(\gamma+\alpha\mu)/\mu(\mu+\gamma)$ gives $\Re_0$.

3.6. *Local stability of disease-free equilibrium*

Proposition 3.1 The disease free equilibrium point is locally asymptotically stable if $\Re_0 < 1$ and unstable if $\Re_0 > 1$.

Proof To proof the proposition we first construct a Jacobean matrix for the system (1)-(5) at DFE

$$J_{E_0} = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 & 0 & 0 \\ \gamma & -\mu & 0 & 0 & \delta \\ 0 & 0 & -(\varphi+\theta+d_1+\mu) & 0 & 0 \\ 0 & 0 & \varphi & -(\beta+d_2+\mu) & 0 \\ 0 & 0 & \theta & \beta & -(\delta+\mu) \end{bmatrix}. \quad (24)$$

Now we compute the Jacobean matrix at disease free equilibrium and investigate its stability effect due to the reproduction number $\Re_0$.

From the Jacobean matrix (28), we obtain a characteristic polynomial by evaluating $\det(J_{E_0} - \lambda I) = 0$ as follows.

$$\begin{vmatrix} -(\gamma+\mu)-\lambda & 0 & 0 & 0 & 0 \\ \gamma & -\mu-\lambda & 0 & 0 & \delta \\ 0 & 0 & K_1-\lambda & 0 & 0 \\ 0 & 0 & \varphi & K_2-\lambda & 0 \\ 0 & 0 & \theta & \beta & K_3-\lambda \end{vmatrix} = 0,$$

where $K_1 = -(\varphi+\theta+d_1+\mu)$, $K_2 = -(\beta+d_2+\mu)$ and $K_3 = -(\delta+\mu)$. Therefore, $\lambda_1 = -(\gamma+\mu)$, $\lambda_2 = -\mu$, $\lambda_3 = -(\varphi+\theta+d_1+\mu)$, and

$$(K_2-\lambda)(K_3-\lambda) = 0 \Rightarrow \lambda^2 - (K_2+K_3)\lambda + K_2K_3 = 0$$

By Routh-Huarth criteria

$$a_1 = -(K_2+K_3) = (\beta+d_2+\mu)+(\delta+\mu) > 0,$$
$$a_2 = K_2K_3 = (\beta+d_2+\mu)(\delta+\mu) > 0.$$

All the eigen values of the Jacobean matrix at disease free equilibrium point are strictly negative. Therefore, the DFE point E_0 is locally asymptotically stable if and only if $\Re_0 < 1$. Hence the proposition is proved. ■

3.7. *Global stability of disease free equilibrium*

In this section, we analyze the global stability of the disease free equilibrium point by applying the technique used in [12]. We write the model equation (1)-(5) in the form:

$$\begin{cases} \dfrac{dX_s}{dt} = A(X_s - X_{DFE,s}) + A_1X_i, \\ \dfrac{dX_i}{dt} = A_2X_i, \end{cases}$$

where X_s is the vector representing the non-transmitting compartment and X_i is the vector representing the transmitting compartments. The disease free equilibrium is globally asymptotically stable if A has negative eigen values and A_2 is a Metzler matrix (i.e., the off-diagonal elements of A_2 are non-negative).

For the model equation (1)-(5) we have $X_s = (P,S,R)^T$ and $X_i = (A,C)^T$, where the superscript T refers to a transpose of the matrix.

We need to check whether a matrix A for non-transmitting compartments has real negative eigen values and that A_2 is Metzler matrix. From the equation for non-transmitting compartments in the model we can get:

$$A = \begin{bmatrix} -(\gamma+\mu) & 0 & 0 \\ \gamma & -\mu & \delta \\ 0 & 0 & -(\delta+\mu) \end{bmatrix}.$$

From the matrix A above, we get the eigen values $\lambda_1 = -(\gamma+\mu)$, $\lambda_2 = -\mu$ and $\lambda_3 = -(\delta+\mu)$ all are real and negative. This implies that the system

$$\frac{dX_s}{dt} = A(X_s - X_{DFE,s}) + A_1X_i$$

is locally and globally asymptotically stable at disease free equilibrium if A_2 is Metzler matrix.

Using suitable rearrangement, we get

$$A_2 = \begin{bmatrix} \rho\varepsilon_1 S^* - (\varphi + \theta + d_1 + \mu) & \rho\varepsilon_2 S^* \\ \rho\varepsilon_2 S^* + \varphi & (1-\rho)\varepsilon_2 S^* - (\beta + d_2 + \mu) \end{bmatrix} \text{ and } A_1 = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ \theta & \beta \end{bmatrix}.$$

Since the off-diagonal elements of A_2 are non-negative so A_2 is a Metzler matrix. Hence, the DFE point is globally asymptotically stable.

Lemma 3.2 For $\Re_0 > 1$, a unique endemic equilibrium point E^* exists and no endemic otherwise.

Proof The endemic equilibrium point denoted by $E^* = (P^*, S^*, A^*, C^*, R^*)$ and it occurs when the disease persists in the community.

For the disease to be endemic, $\frac{dA}{dt} > 0$ and $\frac{dC}{dt} > 0$ that is:

$$\frac{dA}{dt} = \rho\lambda S - (\varphi + \theta + d_1 + \mu) A > 0, \tag{25}$$

$$\frac{dC}{dt} = (1-\rho)\lambda S + \varphi A - (\beta + d_2 + \mu) C > 0. \tag{26}$$

From inequality (26) we get

$$(\beta + d_2 + \mu) C < (1-\rho)\lambda S + \varphi A$$

$$\Rightarrow C < \frac{(1-\rho)\lambda S + \varphi A}{\beta + d_2 + \mu} \tag{27}$$

From inequality (25) we get

$$A < \frac{\rho\lambda S}{\varphi + \theta + d_1 + \mu} \tag{28}$$

$$\Rightarrow \varphi A < \frac{\rho\lambda S\varphi}{\varphi + \theta + d_1 + \mu}$$

$$\Rightarrow \frac{\varphi A}{\beta + d_2 + \mu} < \frac{\rho\lambda S\varphi}{(\varphi + \theta + d_1 + \mu)(\beta + d_2 + \mu)} \tag{29}$$

From (27) we have

$$C < \frac{(1-\rho)\lambda S + \varphi A}{\beta + d_2 + \mu} = \frac{(1-\rho)\lambda S}{\beta + d_2 + \mu} + \frac{\varphi A}{\beta + d_2 + \mu}$$

$$< \frac{(1-\rho)\lambda S}{\beta + d_2 + \mu} + \frac{\rho\lambda S\varphi}{(\beta + d_2 + \mu)(\varphi + \theta + d_1 + \mu)}$$

$$\Rightarrow \varepsilon_2 C < \frac{\varepsilon_2(1-\rho)\lambda S}{\beta + d_2 + \mu} + \frac{\varepsilon_2\rho\lambda S\varphi}{(\beta + d_2 + \mu)(\varphi + \theta + d_1 + \mu)} \tag{30}$$

From (28) we have

$$A < \frac{\rho\lambda S}{\varphi + \theta + d_1 + \mu}$$

$$\Rightarrow \varepsilon_1 A < \frac{\rho\varepsilon_1}{\varphi + \theta + d_1 + \mu} \tag{31}$$

Combining (30) and (31) we get

$$\varepsilon_1 A + \varepsilon_2 C < \frac{\rho\varepsilon_1\lambda S}{\varphi + \theta + d_1 + \mu} + \frac{\varepsilon_2(1-\rho)\lambda S}{\beta + d_2 + \mu} + \frac{\varepsilon_2\rho\lambda S\varphi}{(\beta + d_2 + \mu)(\varphi + \theta + d_1 + \mu)}$$

$$= \lambda S\left[\frac{\varepsilon_1\rho}{\varphi+\theta+d_1+\mu}+\frac{\varepsilon_2(1-\rho)}{\beta+d_2+\mu}+\frac{\varepsilon_2\rho\varphi}{(\beta+d_2+\mu)(\varphi+\theta+d_1+\mu)}\right]$$

$$\Rightarrow \lambda < \lambda S\left[\frac{\varepsilon_1\rho}{\varphi+\theta+d_1+\mu}+\frac{\varepsilon_2(1-\rho)}{\beta+d_2+\mu}+\frac{\varepsilon_2\rho\varphi}{(\beta+d_2+\mu)(\varphi+\theta+d_1+\mu)}\right]$$

$$\Rightarrow 1 < S\left[\frac{\varepsilon_1\rho}{\varphi+\theta+d_1+\mu}+\frac{\varepsilon_2(1-\rho)}{\beta+d_2+\mu}+\frac{\varepsilon_2\rho\varphi}{(\beta+d_2+\mu)(\varphi+\theta+d_1+\mu)}\right]$$

Since $S < S_0 = \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)}$, we have

$$1 < \frac{\Lambda(\gamma+\alpha\mu)}{\mu(\mu+\gamma)}\left[\frac{\varepsilon_1\rho}{\varphi+\theta+d_1+\mu}+\frac{\varepsilon_2(1-\rho)}{\beta+d_2+\mu}+\frac{\varepsilon_2\rho\varphi}{(\beta+d_2+\mu)(\varphi+\theta+d_1+\mu)}\right]$$

$$\Rightarrow \Re_0 > 1$$

Thus, a unique endemic equilibrium exists when $\Re_0 > 1$. ■

3.8. *Global stability of endemic equilibrium point* (*EE*)

Theorem 3.3 If $\Re_0 > 1$, the endemic equilibrium point E^* of the model is globally asymptotically stable.

Proof To prove the global asymptotic stability of the endemic equilibrium point we use the method of Lyapunov function. Define

$$L(P^*,S^*,A^*,C^*,R^*) = \left(P-P^*-P^*\ln\frac{P^*}{P}\right)+\left(S-S^*-S^*\ln\frac{S}{S^*}\right)+\left(A-A^*-A^*\ln\frac{A}{A^*}\right)$$
$$+\left(C-C^*-C^*\ln\frac{C}{C^*}\right)+\left(R-R^*-R^*\ln\frac{R}{R^*}\right).$$

By direct calculating the derivative of L along the solution of the system (1)-(5) we get

$$\frac{dL}{dt} = \left(\frac{P-P^*}{P}\right)\frac{dP}{dt}+\left(\frac{S-S^*}{S}\right)\frac{dS}{dt}+\left(\frac{A-A^*}{A}\right)\frac{dA}{dt}+\left(\frac{C-C^*}{C}\right)\frac{dC}{dt}+\left(\frac{R-R^*}{R}\right)\frac{dR}{dt}$$
$$= \left(\frac{P-P^*}{P}\right)[(1-\alpha)\Lambda-(\gamma+\mu)P]+\left(\frac{S-S^*}{S}\right)[\alpha\Lambda+\gamma P+\delta R-(\lambda+\mu)S]$$

$$+\left(\frac{A-A^*}{A}\right)\left[\rho\lambda S-(\varphi+\theta+d_1+\mu)A\right]+\left(\frac{C-C^*}{C}\right)\left[(1-\rho)\lambda S+\varphi A-(\beta+d_2+\mu)C\right]$$
$$+\left(\frac{R-R^*}{R}\right)[\theta A+\beta C-(\mu+\delta)R]$$

$$\Rightarrow \frac{dL}{dt} = \left(1-\frac{P^*}{P}\right)[(1-\alpha)\Lambda-(\gamma+\mu)P]+\left(1-\frac{S^*}{S}\right)[\alpha\Lambda+\gamma P+\delta R-(\lambda+\mu)S]$$

$$+\left(1-\frac{A^*}{A}\right)\left[\rho\lambda S-(\varphi+\theta+d_1+\mu)A\right]+\left(1-\frac{C^*}{C}\right)\left[(1-\rho)\lambda S+\varphi A-(\beta+d_2+\mu)C\right]$$
$$+\left(1-\frac{R^*}{R}\right)[\theta A+\beta C-(\mu+\delta)R]$$

$$\Rightarrow \frac{dL}{dt} = G - F$$

where

$$G = (\gamma + \mu)P^* + (\lambda + \mu)S^* + (\varphi + \theta + d_1 + \mu)A^* + (\beta + d_2 + \mu)C^* + (\mu + \delta)R^*$$

and

$$F = d_1 A + d_2 C + (1-\alpha)\Lambda \tfrac{P^*}{P} + (\gamma P + \delta R)\tfrac{S^*}{S} + \rho\lambda S \tfrac{A^*}{A} + [(1-\rho)\lambda S + \varphi A]\tfrac{C^*}{C} + [\theta A + \beta C]\tfrac{R^*}{R}.$$

Thus if $G < F$ then $dL/dt \le 0$. Noting that $dL/dt = 0$ if and only if $P = P^*$, $S = S^*$, $A = A^*$, $C = C^*$ and $R = R^*$.

Therefore, the largest compact invariant set in $\Omega = \{(P,S,A,C,R) \in \Omega : dL/dt = 0\}$ is the singleton E^* by Lasalle invariant principle [5] it implies that the endemic equilibrium point is globally asymptotically stable in Ω if $G < F$. ■

4. Sensitivity analysis

The total human mortality and morbidity attributable to HCV disease can be best reduced by investigating the relative importance of the parameters featuring in the basic reproduction number. To determine how best we can do in order to reduce mortality and morbidity due to HCV disease, it is crucial to know the relative importance of different factors responsible for its transmission and prevalence.

Sensitivity analysis was carried out to determine the model robustness to parameter values. This will help us in identifying and verifying model parameters that most influence the pathogen fitness threshold for the pathogens. Further, values obtained for sensitivity indexes indicate which parameters should be targeted most for intervention purposes. Sensitivity analysis of $\Re_0$ with respect to each parameter. The sensitivity analysis of the parameters can be calculated as follows:

$$\Lambda^{\Re_0} = \frac{\partial \Re_0}{\partial \Lambda} \times \frac{\Lambda}{\Re_0} = +1,$$

$$\gamma^{\Re_0} = \frac{\partial \Re_0}{\partial \gamma} \times \frac{\gamma}{\Re_0} = +0.41.$$

Similarly, we can get the sensitivity index of each parameter.

Table 1. Sensitivity index table.

Parameter	Sensitivity Index
Λ	+ve
γ	+ve
ε_1	+ve
ε_2	+ve
φ	+ve
μ	-ve
d_1	-ve
d_2	-ve
θ	-ve
β	-ve

Table 1 shows the sensitivity indices of $\Re_0$ to the parameter for HCV model, evaluated

based on the values on Table 2. The parameters are ordered from the most sensitive to least sensitive. This result shows that, when the parameters values of Λ, γ, ε_1, ε_2 and φ increases while the other are kept constant they increase the value of $\Re_0$ which implies they increases the endemicity of the disease. Whereas the parameters μ, d_1, d_2, θ and β decrease the value of $\Re_0$ while the other are kept constant which implies they decrease the endemicity of the disease.

Table 2. Parameter values for typhoid fever model.

Parameter symbol	Parameter description	Value	Source
Λ	Recruitment rate	100	[1]
α	Proportion of susceptible individuals at birth	0.1	Assumed
μ	Natural mortality rate	0.0004	[1]
d_1	The disease induced mortality rate due to acute infection	0.03	Assumed
d_2	The disease induced mortality rate due to chronic infection	0.05	Assumed
β_1	Effective contact rate of individuals with acute infected	0.002	Assumed
β_2	Effective contact rate of individuals with chronic HCV infected	0.001	Assumed
ρ	The probability at which the susceptible joining into acute infected	0.65	Assumed
γ	Rate of loss of protection	0.35	Assumed
β	The rate of treatment of chronically infected and joining recovered class	0.3	Assumed
δ	Removal rate from recovered subclass to susceptible subclass	0.05	[1]
θ	The rate of treatment of acute infected and joining recovered class	0.23	[1]
φ	The rate at which acute infected individuals become chronically infected	0.05	[1]

5. Extension into an optimal control

In this section we apply optimal control method for the system (1)-(5) by using Pontryagin's maximum principle. The optimal control model is an extension of HCV model by incorporating the following three controls mentioned below.

i. u_1 is the prevention effort, that protect susceptible from contracting the disease.

ii. u_2 is the treatment used for acute infected individuals.

iii. u_3 is the treatment used for chronic infected individuals.

After incorporating u_1, u_2 and u_3 in HCV model (1)-(5), we get the following optimal model of HCV disease.

$$\begin{cases} \dfrac{dP}{dt} = (1-\alpha)\Lambda - (\gamma+\mu)P, \\ \dfrac{dS}{dt} = \alpha\Lambda + \gamma P + \delta R - (1-u_1)\lambda S - \mu S, \\ \dfrac{dA}{dt} = \rho(1-u_1)\lambda S - (\theta+u_2)A - (1-u_2)\varphi A - (d_1+\mu)A, \\ \dfrac{dC}{dt} = (1-\rho)(1-u_1)\lambda S + (1-u_2)\varphi A - (\beta+u_3)C - (d_2+\mu)C, \\ \dfrac{dR}{dt} = (\theta+u_2)A + (\beta+u_3)C - (\mu+\delta)R. \end{cases} \tag{36}$$

The control functions, $u_1(t)$, $u_2(t)$ and $u_3(t)$ are bounded, Lebesgue integrable functions, which is defined as

$$U = \left\{ (u_1(t), u_2(t), u_3(t)) : 0 \le u_1(t) < 1,\ 0 \le u_2(t) < 1,\ 0 \le u_3(t) < 1,\ 0 \le t \le T \right\}.$$

Our aim is to obtain a control U, and P, S, A, C and R that minimized the proposed objective function J and the form of objective functional is taken in line with the literature on epidemic model [17], given by:

$$J = \min_{u_1,u_2,u_3} \int_0^{t_f} \left(b_1 A + b_2 C + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2 \right) dt, \tag{37}$$

where b_1, b_2 and w_i are positive. The expression $\frac{1}{2}w_i u_i^2$ represents costs which is associated with the controls u_i and t_f is the final time. The coefficients are balancing cost factors. Now we seek to find an optimal triple control u_1^*, u_2^* and u_3^*, such that

$$J(u_1^*, u_2^*, u_3^*) = \min\left\{ J(u_1, u_2, u_3) : u_1, u_2, u_3 \in U \right\}, \tag{38}$$

where $U = \left\{ J(u_1, u_2, u_3) \right\}$ is a measurable set and $t \in [0, t_f]$ for the control set.

5.1. *Existence of an optimal control*

The necessary condition that an optimal solution must satisfy comes from maximum principle [15]. The existence of an optimal control pair can be proved by using the results [4].

The system of equation (1)-(5) is bounded by a linear system for a finite time interval so that the existence of linear system is guaranteed [4, Theorem 4.1, p68-69] (see the detail of the proof).

For the optimal control problems, we need to check the following properties are satisfied.

(1) The set of controls and corresponding state variables is non-empty.
(2) The control set U is convex and closed.
(3) The RHS of the state system (1)-(5) is bounded by a linear function in the state and control.
(4) The integrand of the objective functional is concave on U.
(5) The function is bounded below by $a_2 - a_1\left(u_1^2 + u_2^2 + u_3^2\right)^{\frac{a}{2}}$ where $a_1 > 0$, $a_2 > 0$ and $\alpha > 1$.

The existence result in [8, 1982, Theorem 9.2.1, p 182] for the system (1)-(5) with bounded coefficients is used to satisfy condition 1. The control set U is convex and closed by

definition.

The RHS of the state system (1)-(5) satisfies condition 3 as the state solutions are a priori bounded. The integrand in the objective functional $b_1A + b_2C + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2$ is clearly concave on U. Finally, there are $a_1 > 0$, $a_2 > 0$ and $\alpha > 1$ satisfying

$$b_1A + b_2C + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2 \le a_2 - a_1\left(u_1^2 + u_2^2 + u_2^2\right)^{\frac{a}{2}},$$

because the state variables are bounded. Hence, there exist an optimal control (u_1, u_2, u_3) that minimize the objective functional, $J(u_1, u_2, u_3)$.

5.2. *Hamiltonian and optimality system*

The necessary condition for the optimal pair is obtained using the "Pontryagin's maximum principle" ([15]). Therefore, using this principle, we get a Hamiltonian which is defined as

$$H(P,S,A,C,R,t) = L\left(A,C,u_1,u_2,u_3,t\right) + \lambda_1\frac{dP}{dt} + \lambda_2\frac{dS}{dt} + \lambda_3\frac{dA}{dt} + \lambda_4\frac{dC}{dt} + \lambda_5\frac{dR}{dt},$$

where $L\left(A,C,u_1,u_2,u_3,t\right) = b_1A + b_2C + \frac{1}{2}\sum_{i=1}^{3} w_i u_i^2$, and λ_i is adjoint variable to be determined suitably by using Pontryagin's maximum principle.

Theorem 5.1 For an optimal control set u_1, u_2 and u_3 that minimizes J over U there are an adjoint variables $\lambda_1, \lambda_2, ..., \lambda_5$ such that

$$\begin{cases} \frac{d\lambda_1}{dt} = \lambda_1\left(\gamma u_1 + \mu\right) - \lambda_2\gamma u_1, \\ \frac{d\lambda_2}{dt} = \lambda_2\left[\mu + \left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right)\right] - \lambda_3\rho\left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right) \\ \qquad - \lambda_4(1-\rho)\left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right), \\ \frac{d\lambda_3}{dt} = -b_1 + \lambda_2\left(1-u_1\right)\varepsilon_1 S - \lambda_3\left[\rho\varepsilon_1\left(1-u_1\right)S - \left(\theta + u_2\right) - \left(1-u_2\right)\varphi - \left(d_1 + \mu\right)\right] \\ \qquad - \lambda_4\left[(1-\rho)\left(1-u_1\right)\varepsilon_1 S + \left(1-u_2\right)\varphi\right] - \lambda_5\left(\theta + u_2\right), \\ \frac{d\lambda_4}{dt} = -b_2 + \lambda_2\left(1-u_1\right)\varepsilon_2 S - \lambda_3\rho\varepsilon_2\left(1-u_1\right)S - \lambda_4\left[(1-\rho)\varepsilon_2\left(1-u_1\right)S\right. \\ \qquad \left. - \left(u_3 + \beta + d_2 + \mu\right)\right] - \lambda_5\left(\beta + u_3\right), \\ \frac{d\lambda_5}{dt} = -\lambda_2\delta - \lambda_5(\mu + \delta), \end{cases} \tag{39}$$

with transversality conditions $\lambda_i(t_f) = 0$, $i = 1,2,\ldots 5$. Furthermore, we obtained the control set $\left(u_1^*, u_2^*, u_3^*\right)$ characterized by $\partial H / \partial u_i^* = 0$ for $i = 1,2,3$. Hence we obtain

$$u_1^*(t) = \max\left\{0, \min\left(1, \sigma_1\right)\right\},$$
$$u_2^*(t) = \max\left\{0, \min\left(1, \sigma_2\right)\right\},$$
$$u_3^*(t) = \max\left\{0, \min\left(1, \sigma_3\right)\right\},$$

where

$$\sigma_1 = \left[\lambda_1 yP + S\left(\varepsilon_1 A + \varepsilon_2 C\right)\left(-\lambda_2 + \lambda_3\rho + \lambda_4(1-\rho)\right)\right] / w_1,$$

$$\sigma_2 = A\left[\lambda_3(1-\varphi) - \lambda_4\rho - \lambda_5\right]/w_2 ,$$

and $\sigma_3 = c\left(\lambda_4 - \lambda_5\right)/w_3$.

Proof The adjoint variables and transversality conditions are standard results of Pontryagin's maximum principle. To obtain the adjoint equations we differentiate the Hamiltonian H with respect to the state variables P, S, A, C and R respectively and then we obtain

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial P} = \lambda_1\left(\gamma u_1 + \mu\right) - \lambda_2\gamma u_1 ,$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial S} = \lambda_2\left[\mu + \left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right)\right] - \lambda_3\rho\left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right)$$
$$- \lambda_4(1-\rho)\left(1-u_1\right)\left(\varepsilon_1 A + \varepsilon_2 C\right),$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial A} = -b_1 + \lambda_2\left(1-u_1\right)\varepsilon_1 S - \lambda_3\left[\rho\varepsilon_1\left(1-u_1\right)S - \left(\theta + u_2\right) - \left(1-u_2\right)\varphi - \left(d_1 + \mu\right)\right]$$
$$- \lambda_4\left[(1-\rho)\left(1-u_1\right)\varepsilon_1 S + \left(1-u_2\right)\varphi\right] - \lambda_5\left(\theta + u_2\right),$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial C} = -b_2 + \lambda_2\left(1-u_1\right)\varepsilon_2 S - \lambda_3\rho\varepsilon_2\left(1-u_1\right)S - \lambda_4\left[(1-\rho)\varepsilon_2\left(1-u_1\right)S\right.$$
$$\left. - \left(u_3 + \beta + d_2 + \mu\right)\right] - \lambda_5\left(\beta + u_3\right),$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial R} = -\lambda_2\delta - \lambda_5(\mu + \delta).$$

Again using the method of Pontryagin et.al [15], we obtain the controls by solving $\partial H/\partial u_i^* = 0$ for $i = 1,2,3$ then

$$u_1^* = \left[\lambda_1 yP + S\left(\varepsilon_1 A + \varepsilon_2 C\right)\left(-\lambda_2 + \lambda_3\rho + \lambda_4(1-\rho)\right)\right]/w_1 ,$$
$$u_2^* = A\left[\lambda_3(1-\varphi) - \lambda_4\rho - \lambda_5\right]/w_2 ,$$
$$u_3^* = c\left(\lambda_4 - \lambda_5\right)/w_3 .$$

Thus, writing u_1^*, u_2^* and u_3^* using standard control arguments involving the bounds on the controls, we conclude

$$u_1^* = \begin{cases} 0 & \text{if} \quad \sigma_1 \le 0, \\ \sigma_1 & \text{if} \quad 0 < \sigma_1 < 1, \\ 1 & \text{if} \quad \sigma_1 \ge 1. \end{cases} \qquad u_2^* = \begin{cases} 0 & \text{if} \quad \sigma_2 \le 0, \\ \sigma_2 & \text{if} \quad 0 < \sigma_2 < 1, \\ 1 & \text{if} \quad \sigma_2 \ge 1. \end{cases} \qquad u_3^* = \begin{cases} 0 & \text{if} \quad \sigma_3 \le 0, \\ \sigma_3 & \text{if} \quad 0 < \sigma_3 < 1, \\ 1 & \text{if} \quad \sigma_3 \ge 1. \end{cases}$$

This implies

$$u_1^* = \max\left\{0, \min\left(1, \sigma_1\right)\right\},$$
$$u_2^* = \max\left\{0, \min\left(1, \sigma_2\right)\right\},$$
$$u_3^* = \max\left\{0, \min\left(1, \sigma_3\right)\right\},$$

The optimality system is formed from the optimal control system and the adjoint variable system by incorporating the characterized control set and initial and transversality condition.

$$
\begin{cases}
\dfrac{dP}{dt} = (1-\alpha)\Lambda - \gamma u_1 P - \mu P, \\
\dfrac{dS}{dt} = \alpha\Lambda + \gamma u_1 P + \delta R - (1-u_1)\lambda S - \mu S, \\
\dfrac{dA}{dt} = \rho(1-u_1)\lambda S - (\theta + u_2)A - (1-u_2)\varphi A - (d_1+\mu)A, \\
\dfrac{dC}{dt} = (1-\rho)(1-u_1)\lambda S + (1-u_2)\varphi A - (\beta + u_3)C - (d_2+\mu)C, \\
\dfrac{dR}{dt} = (\theta + u_2)A + (\beta + u_3)C - (\mu+\delta)R, \\
\dfrac{d\lambda_1}{dt} = \lambda_1(\gamma u_1 + \mu) - \lambda_2 \gamma u_1, \\
\dfrac{d\lambda_2}{dt} = \lambda_2\left[\mu + (1-u_1)(\varepsilon_1 A + \varepsilon_2 C)\right] - \lambda_3\rho(1-u_1)(\varepsilon_1 A + \varepsilon_2 C) \\
\quad - \lambda_4(1-\rho)(1-u_1)(\varepsilon_1 A + \varepsilon_2 C), \\
\dfrac{d\lambda_3}{dt} = -b_1 + \lambda_2(1-u_1)\varepsilon_1 S - \lambda_3\left[\rho\varepsilon_1(1-u_1)S - (\theta+u_2) - (1-u_2)\varphi - (d_1+\mu)\right] \\
\quad - \lambda_4\left[(1-\rho)(1-u_1)\varepsilon_1 S + (1-u_2)\varphi\right] - \lambda_5(\theta+u_2), \\
\dfrac{d\lambda_4}{dt} = -b_2 + \lambda_2(1-u_1)\varepsilon_2 S - \lambda_3\rho\varepsilon_2(1-u_1)S - \lambda_4\left[(1-\rho)\varepsilon_2(1-u_1)S \right. \\
\quad \left. -(u_3+\beta+d_2+\mu)\right], \\
\dfrac{d\lambda_5}{dt} = -\lambda_2\delta - \lambda_5(\mu+\delta),
\end{cases}
\tag{40}
$$

such that $\lambda_i(t_f) = 0,\ i = 1,2,\ldots,5,\quad P(0) = P_0,\quad S(0) = S_0,\quad A(0) = A_0,$ $C(0) = C_0$ and $R(0) = R_0.$ ■

6. Numerical simulations

In the present work, we have used PSACR epidemic model with control measures. The simulations are carried out in order to explore the impacts of control measures on the HCV disease dynamics. Following parameter values are used in the model for simulation purpose

$$\Lambda = 100,\ \alpha = 0.1,\ \mu = 0.004,\ d_1 = 0.03,\ d_2 = 0.05,\ \beta_1 = 0.002,\ \beta_2 = 0.001,\ \rho = 165,$$
$$\gamma = 0.35,\ \beta = 0.3,\ \delta = 0.05,\ \theta = 0.23,\ \varphi = 0.05,\ T = 6,\ b_1 = 100,\ b_2 = 50,\ w_1 = 2,$$
$$w_2 = 3,\ w_3 = 5,$$

and initial values $P(0) = 200,\ S(0) = 600,\ A(0) = 180,\ C(0) = 120,\ R(0) = 200.$

The optimal control solution is obtained by solving the optimality system (40), which consists of the state system, the adjoint system and transversality condition. To solve the state system we use a forward fourth-order Runge-kutta method and solve the adjoint system using a backward fourth-order Runge-Kutta method. The solution iterative scheme involves making a guess of the controls and solves the state system using forward fourth order Runge-Kutta scheme. Due to the transversality conditions, the adjoint equations are then solved by the backward fourth-order Runge-Kutta scheme using the current iterations solutions of the state equations. The controls are then updated using a convex combination

of the previous controls and the values obtained using the characterizations. The updated controls are then used to repeat the solution of the state and adjoint systems. This process is repeated until the values in the current iteration are close enough to the previous iteration values [7].

In this section we investigate numerically the effect of the following optimal control strategies on the spread of the disease in a population.

i. Using prevention effort (u_1), that protect susceptible from contracting the disease $(u_2 = 0$ and $u_3 = 0)$.
ii. Using treatment effort (u_2) for acute infected individuals $(u_1 = 0$ and $u_3 = 0)$.
iii. Using treatment effort (u_3) for chronic infected individuals $(u_1 = 0$ and $u_2 = 0)$.
iv. Using prevention (u_1) for susceptible and treatment (u_2) for acute infected individuals $(u_3 = 0)$.
v. Using prevention (u_1) for susceptible and treatment (u_3) for chronic infected individuals $(u_2 = 0)$.
vi. Using treatment (u_2) for acute and treatment (u_3) for chronic infected individuals $(u_1 = 0)$.
vii. Using all the three controls, prevention effort (u_1), treatment effort (u_2) and treatment effort (u_3).

6.1. *Control with prevention only*

In Figure 3, we observe that due to the implementation of prevention effort on susceptible population the proportion of acute and chronic infected population decreases as compared with the case without control. This implies prevention minimizes the rate of joining individuals in to acute and chronic compartments. Thus, we can deduce that optimized prevention reduces the burden of the both acute and chronic infection of HCV.

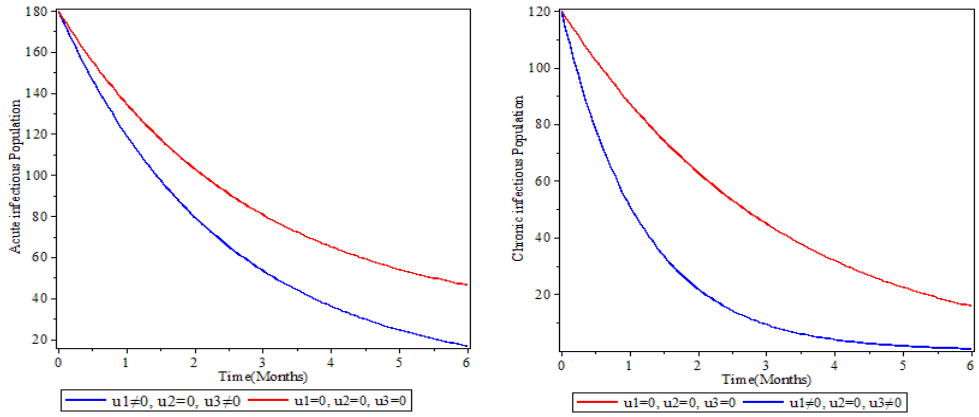

Figure 3. Simulation of optimal control with prevention only.

6.2. *Controls with only treatment for acute infected population* (u_2)

The HCV treatment control u_2 (treatment given for acute infected population) is used to optimize the objective functional J; the other controls (u_1 and u_3) relating to HCV are set to zero. From Figure 4 it is observed that the acute infected population decreases with time

since some of the acute infected population are recruited for treatment and remaining joins the chronic infected class. As the rate of control (u_2) increases, the acute infected population decreases with time leading to the decrease of chronic infected population. As a result it is possible to say applying a control measure on acute infected population leads to a faster reduction of proportion of both acute and chronic infected population as compared to the case without applying the control measure.

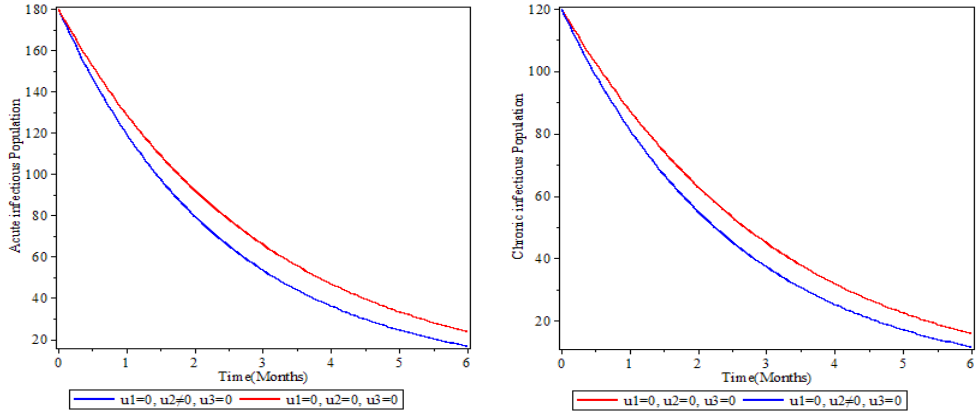

Figure 4. Simulation of optimal control with treatment for acute infectious only.

6.3. *Controls with treatment only for chronic infected population* (u_3)

The HCV treatment control u_3 is used to optimize the objective functional J; the other controls (u_1 and u_2) relating to HCV are set to zero. From Figure 5 we observe that initially the control u_3 has no effect on the dynamics of chronic infected population. In the mean time the proportion of chronic infected population decrease with time leading to faster declining of chronic infected population.

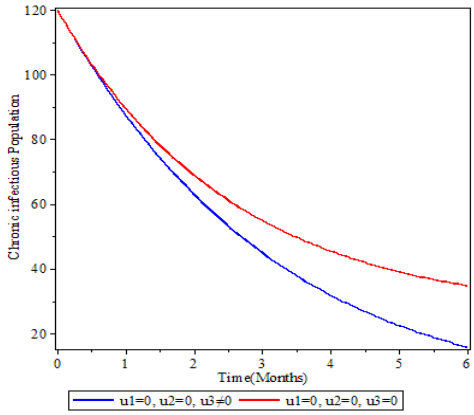

Figure 5. Simulation of optimal control with treatment for chronic infectious only.

6.4. *Controls with prevention and treatment for acute infected population* $(u_1$ *and* $u_2)$

The HCV treatment controls u_1 and u_2 are used to optimize the objective functional J; the other control u_3 relating to HCV is set to zero. We observe from Figure 6 that this

strategy shows there is a significant effect in reducing the proportion of both acute and chronic infected population in than the previous strategies. This situation occurred due to the fact that the control u_1 minimizes both acute and chronic infected population which will join both compartments whereas the control u_2 minimizes the proportion of acute infectious population as a result the chronic infectious population will be minimized.

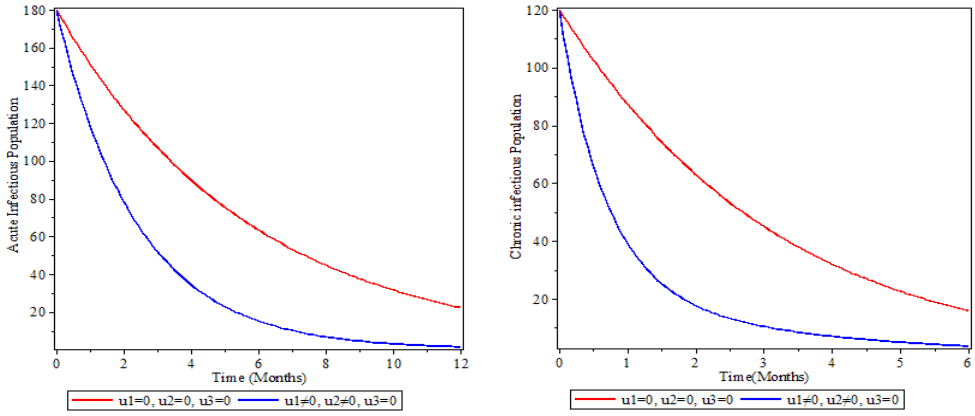

Figure 6. Simulation of optimal control with prevention and treatment for acute infectious.

6.5. *Controls with Prevention and treatment for chronic infected population* (u_1 *and* u_3)

The HCV treatment controls u_1 and u_3 are used to optimize the objective functional J; the other control u_2 relating to HCV is set to zero. We observe from Figure 7 that this strategy shows there is a higher reduction of the proportion of population of chronic infected population than the acute infectious population.

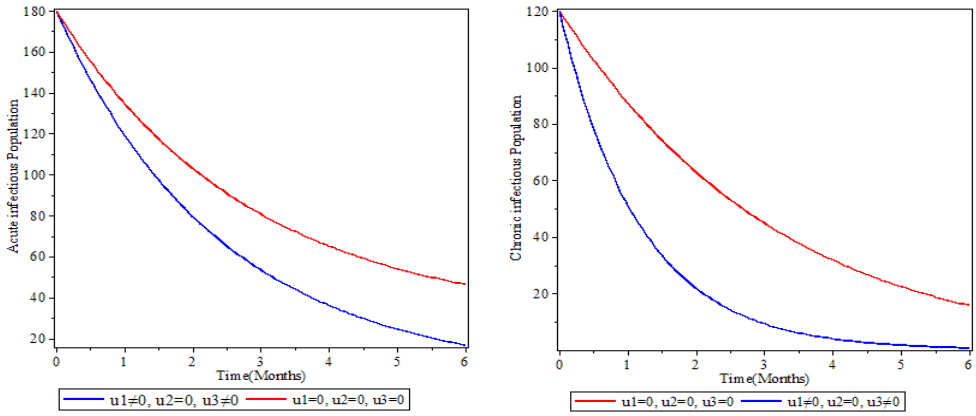

Figure 7. Simulation of optimal control with prevention and treatment for chronic infectious.

6.6. *Controls with prevention and treatment for chronic infected population* (u_2 *and* u_3)

The HCV treatment controls u_2 and u_3 are used to optimize the objective functional J; the other control u_1 relating to HCV is set to zero. We observe from Figure 8 that this strategy shows there is only a slight variation as compared to the case without control. This

occurred due to the fact that the higher recruitment rate of susceptible populations to both acute and chronic compartments.

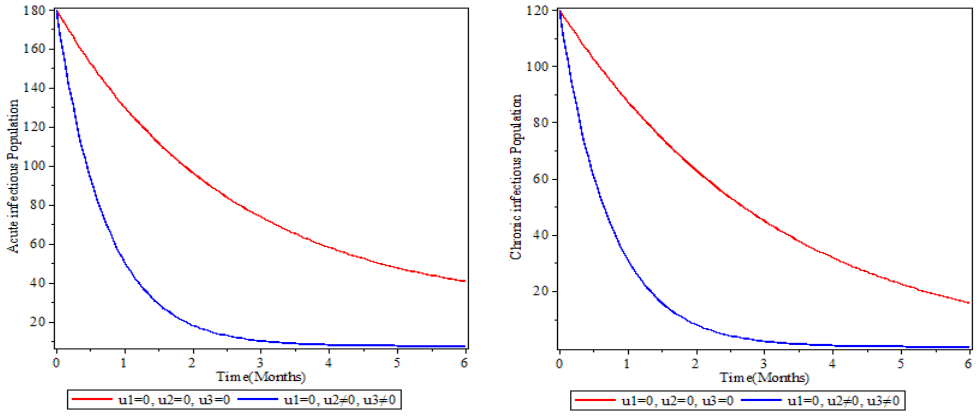

Figure 8. Simulation of optimal control with treatment for acute and chronic infectious.

6.7. *Controls with prevention* (u_1), *treatment* (u_2), *and treatment* (u_3)

Here we used all the three intervention strategies which enable to minimize the objective functional J. We observe from Figure 9 that the proportion of both acute and chronic infectious population vanishes rapidly before the specified time. Therefore, applying this strategy helps to eradicate HCV from the population.

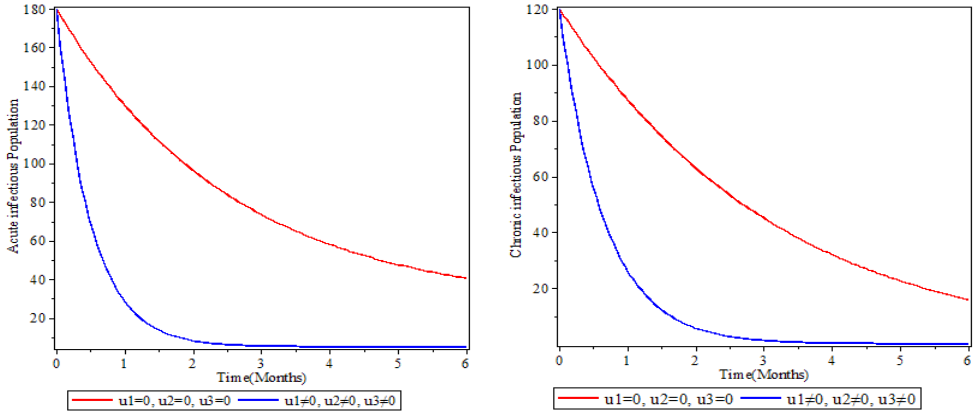

Figure 9. Simulation of optimal control with all the three strategies.

7. Discussions and conclusions

In this study a deterministic mathematical model of HCV consisting acute and chronic stages with optimal control strategies has been established. The model incorporates the assumption that all populations are equally susceptible. Both qualitative and numerical analysis of the model was done. We have shown that there exists a feasible region where the model is well posed and biologically meaningful in which a unique disease free equilibrium point exists. The steady state points were obtained and their local and global stability conditions were investigated. The model has a unique disease free equilibrium if $\Re_0 < 1$ and has endemic equilibrium if $\Re_0 > 1$. Sensitivity analysis of the model was done. It was observed that mortality rate has higher impact in minimizing the burden of

the disease when the parameter increases which is not biologically reasonable to use it as a control mechanism.

For the given model an optimal control problem is formulated by incorporating different control strategies. The optimality condition was established by Pontryagin's maximum principle. A numerical simulation of the model was conducted and different combinations of control strategies were compared. It was observed that prevention has a significant impact in minimized the burden of the disease. It was also shown that treatments given for acute and chronic infected population minimizes the burden of the disease. Finally, it was observed that applying all the three control strategies eliminate HCV disease from the population.

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