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RESEARCH PAPER

Analyses of Hepatitis C Virus with Targeted Treatment for Chronic Infections: Mathematical Modeling Perspective

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Abstract

This paper examined the spread of hepatitis C virus (HCV) infection among population of chronically infected individuals receiving treatment. The model classifies individuals into five categories: susceptible, acutely infected, chronically infected, treated, and recovered, and is governed by a system of nonlinear ordinary differential equations. The qualitative analysis focuses on key solution properties such as positivity, boundedness, existence, uniqueness, and the stability of the disease-free equilibrium, along with a sensitivity analysis. MATLAB simulations provide additional insights into the progression of the infection. The study findings highlight the potential of timely intervention, using either direct-acting antivirals (DAAs) or natural herbal supplements under medical guidance, to significantly reduce the duration of chronic HCV infection and ultimately eliminate the virus.

Keywords: acute, chronic, hepatitis c virus, model, reproduction number, sensitivity analysis

Introduction

Hepatitis C virus (HCV) is transmitted through blood-borne infection that inflames and damages the liver, significantly increasing the risk of liver cancer. While the virus may start with a seemingly minor infection, it can progress to chronic diseases such as cancer and liver cirrhosis. Despite being identified in 1989, it has now grown into a serious threat to public health (Shi, R., and Cui, Y. 2016). The virus is transmitted through various routes, including the sharing of contaminated needles and other drug paraphernalia, unsafe blood transfusions, and unprotected sexual contact (Sadki *et al.,* 2023). According to recent WHO report, approximately 185 million people worldwide are affected with HCV. Of these, around 85% develop chronic infections, while experience acute infections. HCV is responsible for an estimated 350,000 deaths each year, and currently, there is no vaccine available to prevent hepatitis C infection. In Australia, direct-acting antivirals (DAAs) have been introduced for the treatment of chronic hepatitis C, offering high cure rates with minimal side effects (Nguyen *et al.,* 2023). While DAAs represent a significant improvement, the "one-size-fits-all" approach has its limitations. The DAAs industry is increasingly recognizing the importance of personalized medicine, tailoring treatment to individual patient characteristics for optimal outcomes (Nguyen *et al.,* 2023).

Mathematical models are powerful tools; they don't just predict, they can also guide research. They help us pinpoint crucial biological factors that need more investigation and suggest changes in behavior or medical care that could improve patient results. HCV, for instance, is a major public health concern because it can lead to severe complications. Yet, surprisingly little attention has been given to developing mathematical models to understand how HCV spreads within communities. Ahmed *et al.* (2022) investigated the dynamic of HCV using a fractal-fractional model, analyzing both local and global stability of the disease. Similarly, Elbasha (2013) developed a mathematical model to study how HCV spreads and how antiviral treatments affect its spread. Their model indicated that higher treatment rates with

more effective drugs, resulting in faster cures and fewer treatment failures, would significantly reduce the number of new infections and the overall impact of the disease.

The researchers also highlighted the importance of reinfection in understanding HCV transmission and the effectiveness of treatment. They concluded that highly effective treatments have the potential to significantly reduce the burden of HCV on public health. Ayobami (2020) developed a mathematical model to study HCV transmission, incorporating treatment and other control measures. The model showed that early intervention, including education, awareness campaigns, and intensive treatment at the initial stages of an outbreak could significantly reduce or even eradicate HCV. Mushayabasa (2014) assessed the impact of antiviral therapy, abstinence, and relapse on the spread of HCV, simulating the long-term dynamics of HCV cases over a 50-year period. The model suggested that increasing abstinence rates and reducing relapse rates could significantly reduce HCV transmission among intravenous drug users. Additionally, Shi, R., and Cui, Y. (2016) studied a mathematical model that examines the transmission of HCV, incorporating both chronic primary infection and the possibility of reinfection.

A fractional-order differential mathematical model was used to analyze the dynamics of HCV infection, considering both virus-to-cell and cell-to-cell transmission pathways, along with a rate of cure for infected cells (Sadki *et al.,* 2023). Martin *et al*. (2011) focused on HCV transmission among injecting drug users, demonstrated that the effectiveness of antiviral treatment is remains strong even in the presence of uncertainties regarding immunity. This suggests that treatment remains a crucial factor in controlling the spread of HCV, regardless of immune factors. In a study by Jia *et al*. (2019), a new model was proposed to understand how HCV spreads in China. Their model showed that the main way the virus spreads is through contact with people who are infected. They suggested several ways to stop the virus's spread, including reducing transmission through contact with infected individuals and speeding up virus detection. Additionally, they mentioned the importance of faster treatment and improving recovery rates for hospitalized patients. Rihan *et al*. (2017) established a mathematical model using a fractional-order derivative to analyze the dynamics of HCV replication. The model incorporated the effects of interferon-alpha (IFN) treatment and accounted for intermediate cellular interactions and delays in the viral life cycle.

The mathematical model presented by Pitcher *et al*. (2019) suggests that prioritizing treatment for individuals with advanced liver disease, while focusing interventions on incarcerated individuals and their injection network partners, could be crucial in eliminating HCV among individuals who vaccinate drugs. Chatterjee *et al.* (2021) used a mathematical model to explore how HCV infection spreads and how to control it. Their findings indicated that regular adherence to direct-acting antiviral (DAA) therapy is effective in preventing the disease, and that the duration and frequency of treatment (pulse therapy) significantly impact the progression and replication of HCV. Rong *et al*. (2013) developed a sophisticated multi-scale model that incorporates intracellular viral replication, allowing for the study of how the HCV changes in persistent cured with Direct-Acting Antivirals. Their analysis of data from persistent cured with the new HCV protease inhibitor, danoprevir, indicated that the drug effectively inhibits the virus from replicating and aids in eliminating the existing virus. Avendano (2002) proposed a model showing that increasing the death rate of infected liver cells and the free virus could effectively lower the viral load, based on a system considering uninfected and infected liver cells, HCV, and T-cells. Nguyen *et al.* (2023) studied how to use a different mathematical approach (optimal control theory) to create treatment plans that are specific to each person with HCV. Computer simulations showed that this approach could reduce the amount of virus and the number of infected liver cells, while also allowing healthy liver cells to grow. Using

adaptive neuro-fuzzy technology, Khodaei *et al*. (2002) developed and tested a new intelligent controller aims to effectively control HCV infection within the population. Wameko (2019) modeled the spread of HCV and analyzed the effectiveness of different control strategies, which include preventing new infections, treating acutely infected individuals, and providing treatment for those with chronic infection. The results indicated that the combined application of these strategies could eradicate HCV. Okosun (2014) investigated how optimal control strategies, including screening immigrants and treating HCV, influence disease transmission in a homogeneous population with constant immigration of susceptible individuals. Their research concluded that targeting both acute and chronic infections through treatment is the most effective approach to control HCV spread. Mehr *et al*. (2021) designed a sophisticated mathematical model to track HCV outbreak dynamics. This model accounts for various population groups, including those unaware and aware of their susceptibility, those with acute and chronic infections, and those receiving treatment. El Youssoufi *et al*. (2020) also developed a discrete mathematical model to study HCV infection dynamics and evaluated the effectiveness of various control strategies, particularly in the context of treatment. Their research explored the impact of each control measure and ultimately concluded that the proposed strategies were effective in reducing HCV burden. To determine the best treatment strategy for HCV among active IDUs, Martin et al. (2011) developed a model simulating HCV transmission and treatment over a 10-year period. Khodaei-Mehr *et al*. (2018) used ANFIS-based optimal control and showed that the proposed strategy effectively reduced the number of infected individuals by approximately 19% compared to other control strategies. Imran *et al*. (2014) also investigated the impact of different control strategies on HCV transmission dynamics using a deterministic model. Their analysis revealed that implementing a time-dependent quarantine strategy is the most effective and cost-efficient way to manage the disease. The study by Ainea *et at*. (2012) also revealed that addressing both treatment and the influx of infected immigrants is essential for effectively managing HCV transmission. Their findings emphasize the need to reduce transmission rates within the community to lower long-term prevalence of the disease.

A study by Mahroug and Bentout, (2023) generalized an age-of-infection model for heterogeneous environments. They addressed well-posedness, proving bounded, positive solutions despite the model's partial degeneracy and non-compact solution map. Djilali *et al*. (2024) explored a generalized nonlocal dispersion SIS epidemic model with spatial heterogeneity, subject to Neumann boundary conditions. Their aim is to analyze the model using a convolution operator for nonlocal spatial movement and a generalized incidence function.

Djilali *et al.* (2025) models a process in heterogeneous environments using spatiotemporal methods and distributed delay. The study by Din *et al*. (2021) examined the existence of a stationary Markov process in degenerate stochastic differential equations. Furthermore, it explores the influence of noise intensity, cell-to-cell infection, and time delays on virus dynamics, using realistic parameter values. tul Ain (2024) introduced a stochastic epidemic model of cholera transmission, designed to analyze long-term dynamics in migrating communities susceptible to pathogen contamination. The model consists of six distinct human and microbial groups, interrelated through mathematical formulas that capture disease traits and environmental noise.

In this article, model that investigates the dynamics of HCV infection among chronically infected individuals receiving treatment was developed and analyzed. The model classifies individuals into five categories such as S(t), C(t), A(t), T(t) and R(t), which stands for susceptible, acutely infected, chronically infected, treated, and recovered, respectively. Our findings demonstrate that rapid identification and treatment of those in chronic stages of HCV infection are key to effective and accelerated elimination. The rest of the paper is organized as follows: Section 2

introduces the mathematical model and the corresponding nonlinear system of ordinary differential equations. Section 3 explains the mathematical analysis of the model. The numerical simulation results and discussion are offered in Sections 4 and 5, with the conclusion delivered in Section 6.

Model Formulations

This model analyzes HCV infection in chronically infected individuals undergoing treatment using a mathematical approach. The model classifies the population at time `t` into distinct epidemiological groups, such as:

- The susceptible group, S(t) represents those in the population who are at risk of contracting HCV,
- The acutely infected class, symbolized by A(t) involves of persons who have newly contracted HCV, are asymptomatic, and may recover spontaneously without treatment,
- Chronically infected persons, symbolized C(t), are those with persistent HCV infection who remain infectious and face a high risk of liver failure or cancer without treatment,
- The treatment class T(t) symbolizes individuals who are actively experiencing treatment for chronic HCV infection, using either Direct-Acting Antivirals or natural herbal supplements. This classes contains those who have not yet succeeded a medication,

The number of recovered individuals at time t, denoted by R(t) represents those in the population who have recovered from HCV infection.

Thus, the total population $N(t)$ is given by

$$N(t) = S(t) + A(t) + C(t) + T(t) + R(t)$$

In order to develop our model; we rely on the following assumptions:

(A1) Individuals in all classes have a mortality rate of μ from causes other than HCV.

(A2) The susceptible S(t) persons are engaged into the population through birth and migration at a constant rate π and get the recovered persons from the recovered class by the rate ω.

(A3) The acute infected A(t) group is increased from susceptible group by $\beta\lambda$ screening rate and decreased by disease induced death rate δ_1.

(A4) The chronic infected C(t) class is increased from susceptible group by $(1-\beta)\lambda$ screening rate, the acute group by the rate Ɛ and also increased by getting some persons from treatment failure rate ρ and decreased by the disease induced death rate δ_2.

(A5) The treatment T(t) class is increased from chronically infected class by the rate progression η and decreased by the disease induced death rate δ_3.

(A6) The recovered R(t) class grows as individuals from the treatment class are cured at a specific cure rate γ.

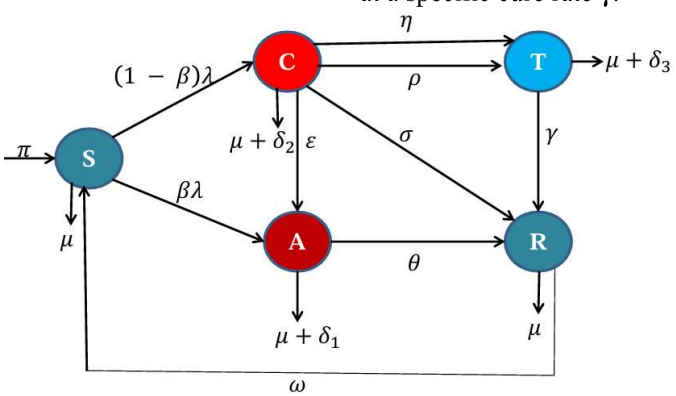

Figure 1: Flow diagram of the HCV infection transmission model, incorporating treatment.

Given the assumptions and the flow diagram (figure 1), we can set up the system of non-linear ordinary differential equations as follows:

$$\frac{dS}{dt} = \pi + \omega R - (\mu + \lambda)S,$$

$$\frac{dA}{dt} = \beta\lambda S - (\varepsilon + \mu + \delta_1 + \theta)A,$$

$$\frac{dC}{dt} = \varepsilon A + (1-\beta)\lambda S + \rho T - (\mu + \delta_2 + \eta + \sigma)C, \quad (1)$$

$$\frac{dT}{dt} = \eta C - (\mu + \gamma + \delta_3 + \rho)T,$$

$$\frac{dR}{dt} = \gamma T + \theta A + \sigma C - (\mu + \omega)R,$$

where $\lambda = \frac{\alpha_1 A + \alpha_2 C}{N}$. Here α_1 is effective contact rate of population with acute HCV and α_2 is effective contact rate of population with chronic HCV. The initial condition of the population is

$S(0) = S_0, A(0) = A_0, C(0) = C_0, T(0) = T_0$ and $R(0) = R_0$

The biological meanings of all parameters are given below in table 1.

Table 1: Description of parameters of model (1)

Parameter	Description
π	New recruits into the population
μ	Natural mortality rate
β	The proportion at which S(t) joining A(t) and C(t)
δ_1	The contribution of disease to mortality in A(t)
δ_2	The contribution of disease to mortality in C(t)
δ_3	The contribution of disease to mortality in T(t)
ε	The rate at which A(t) become C(t)
σ	The recovery rate from C(t)
η	Rate of progression for T(t) from C(t)
p	Treatment failure of C(t)
γ	Treatment cure rate
θ	The rate of A(t) joining R(t)
ω	Removal rate from R(t) to S(t)

Model analyses

Positivity and boundedness of the solution, equilibrium points, reproduction number, stability of disease free equilibrium point and sensitivity analysis will be discussed in this section.

Positivity and Boundedness of the solutions

Since each component of the model represents a population, it's essential to demonstrate that all variables *S(t), A(t), C(t), T(t)* and *R(t)* remain non-negative and bounded for all $t > 0$

Theorem 3.1. (Positivity). If the initial conditions S_0, A_0, C_0, T_0 and R_0, are set for $t_0 > 0$, then for all $t \in (0, t_0)$, the values *S(t), A(t), C(t), T(t) and R(t)* remain positive in R_+^5

Proof. We start with the first equation of the model, which can be expressed as:

$$\frac{dS}{dt} = \pi + \omega R - (\mu + \lambda)S \geq -(\mu + \lambda)S.$$

From this, we derive that:

$S(t) \geq S_0 exp(-\int(\mu + \lambda)dt) > 0$, indicating that S(t) remains non-negative for all t, where S_0 is the initial susceptible population at $t=0$

By applying similar reasoning to the other dynamic variables, we can conclude that they also stay positive for all $t > 0$

$$A(t) \geq A_0 exp\left(-\int_0^t (\varepsilon + \mu + \delta_1 + \theta)\,dt\right) > 0,$$

$$C(t) \geq C_0 exp\left(-\int_0^t (\mu + \delta_2 + \eta + \sigma)\,dt\right) > 0,$$

$$T(t) \geq T_0 exp\left(-\int_0^t (\mu + \delta_3 + \gamma + \rho)\,dt\right) > 0,$$

$$R(t) \geq R_0 exp\left(-\int_0^t (\mu + \omega)\,dt\right) > 0.$$

Thus, for all $t \in [0, t_0)]$, *S(t), A(t), C(t), T(t) and R(t)* are positive in R_+^5.

Theorem 3.2. (Boundedness). For the functions *S(t), A(t), C(t), T(t) and R(t)* there exists a positive constants S_M, A_M, C_M, T_M, *and* R_M such that $\lim_{t\to\infty} \sup S(t) \leq S_M$, $\lim_{t\to\infty} \sup A(t) \leq A_M$, $\lim_{t\to\infty} \sup C(t) \leq C_M$, $\lim_{t\to\infty} \sup T(t) \leq T_M$, and $\lim_{t\to\infty} \sup R(t) \leq R_M$ for all $t \in [0, t_0)]$, $t_0 > 0$.

Proof. To show the boundedness, we add all the equation of proposed model as follows:

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dA}{dt} + \frac{dC}{dt} + \frac{dT}{dt} + \frac{dR}{dt} =$$

$$\pi - \mu N - (\delta_1 A + \delta_2 C\ \delta_3 T).$$

This implies that $\frac{dN}{dt} \leq \pi - \mu N$. It follows that $N(t) \leq \pi\mu + N_0 exp(-\mu t)$. Then by considering $t \to \infty$, we have $\lim_{t\to\infty} \sup N(t) \leq \frac{\pi}{\mu}$. Thus, the model is bounded by taking $S_M = A_M = C_M = T_M = R_M = \frac{\pi}{\mu}$. This completes the proof of theorem.

Theorem 3.3. (Closed region).
The region $\Omega = \{(S,A,C,T,R) \in R_+^5 : S(t) + A(t) + C(t) + T(t) + R(t) \leq \frac{\pi}{\mu}\}$ is a positively invariant region for the model.

Proof. From theorem 3.2, we have $\frac{dN}{dt} \leq \pi - \mu N$, and using the initial condition $N_0 > 0$ along with integrating factor, we derive that $0 \leq N(t) \leq \frac{\pi}{\mu} + N_0 exp(-\mu t)$, where N_0 is the initial total population.

As $t \to \infty, N(t) \leq \frac{\pi}{\mu}$. This shows that all feasible solutions of the system will enter the region Ω, which is positively invariant. Thus, all solutions within Ω will remain there for all $t \geq 0$. Therefore, it suffices to analyze the transmission dynamics of the HCV model system within Ω.

Equilibrium points

Disease free Equilibrium (DFE) point

To find the equilibrium points of the model equations in (1), we solve them simultaneously with the time derivatives set to zero and assume that all dynamic variables are non-zero. This process yields two equilibrium points: one representing a disease-free state and the other an endemic equilibrium. In this context, we focus on determining the disease-free equilibrium point, where the disease compartments are treated as zero. Infected compartments include A, C, T while the others are not infected. At infection free steady state $A = C = T = R = 0$. Hence, the disease - free state is $N_0 = (S_0, A_0, C_0, T_0, R_0)$. By setting right hand side of the system to zero, we get: $N^D = (S^D, A^D, C^D, T^D, R^D) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0\right)$.

Disease endemic equilibrium (DEE) point

Next, we identify the endemic equilibrium point of the system where the disease is present in the population this equilibrium point is found by setting each equation in the system to zero while assuming that all dynamic variables are non-zero $(i.e.\ S^* \neq A^* \neq C^* \neq T^* \neq R^* = 0)$ by solving the system of equations in (1) simultaneously with the time derivatives equal to zero we obtain the expression $N^* = (S^*, A^*, C^*, T^*, R^*)$ where $S^* = \frac{\pi + \omega R^*}{\lambda^* + \mu}$, $A^* = \frac{\beta\lambda^*(\pi + \omega R^*) + \omega R^*}{k_1(\lambda^* + \mu)}$, $C^* = \frac{(\pi + \omega R^*) + (\varepsilon\beta\lambda + (1-\beta)\lambda^* k_1)(k_2 k_3)}{k_1 k_2(\lambda^* + \mu)(k_2 k_3 + \eta\rho)}$, $T^* = \frac{(\pi + \omega R^*) + (\varepsilon\beta\lambda^* + (1-\beta)\lambda^* k_1)(\eta k_2)}{k_1 k_2(\lambda^* + \mu)(k_2 k_3 + \eta\rho)}$ and

$$R^* = \frac{[\pi(\eta\gamma + \sigma k_3) + (\varepsilon\beta\lambda^* + (1-\beta)\lambda^* k_1) + \theta\beta\lambda^*(k_2 k_3 + \eta\rho)]}{k_1(\lambda^* + \mu)(k_2 k_3 + \eta\rho) - \omega[(\eta\gamma + \sigma k_3) + (\varepsilon\beta\lambda^* + (1-\beta)\lambda^* k_1) + \theta\beta\lambda^*(k_2 k_3 + \eta\rho)]}.$$

Here $\lambda^* = \frac{\alpha_1 A^* + \alpha_2 C^*}{N^*}$

$k_1 = \varepsilon + \mu + \delta_1 + \theta, k_2 = \mu + \delta_2 + \eta + \sigma$ and $k_3 = \mu + \delta_3 + \gamma + \rho$.

The symbol $'*'$ denotes the population of each variable at the equilibrium point. Let the population in each class at steady state be represented as S^*, A^*, C^*, T^* and R^*. Consequently, the force of infection at the fixed points, denoted λ^*, corresponds to the non-negative roots of $\lambda^* = \frac{\alpha_1 A^* + \alpha_2 C^*}{N^*}$.

Basic reproduction number

Definition 3.1. The basic reproduction number (R_0) represents the typical number of new infections caused by a single infected individual when introduced into a population where everyone else is susceptible to the disease. It can be calculated using the next-generation approach, a method detailed by Driessche and Watmough in their 2002

publication. To compute R_0, it is essential to differentiate new infections from other transitions within the population. The infected classes are A, C and T. We can express system (1) as $\dot{x} = F(x) - V(x)$, $V = V^- - V^+$, where $x = (A, C, T, S, R)$. Here, F represents the rate of new infections in each class, V^+ is the rate of transfer into each class through other means, and V^- is the rate of transfer out of each class. Given the system of non-linear differential equations

$$\begin{aligned}
\dot{A} &= \beta\lambda S - (\varepsilon + \mu + \delta_1 + \theta)A,\\
\dot{C} &= \varepsilon A + (1-\beta)\lambda S + \rho T - (\mu + \delta_2 + \eta + \sigma)C,\\
\dot{T} &= \eta C - (\mu + \gamma + \delta_3 + \rho)T,\\
\dot{S} &= \pi + \omega R - (\mu + \lambda)S,\\
\dot{R} &= \gamma T + \theta A + \sigma C - (\mu + \omega)R.
\end{aligned} \quad (2)$$

Based on the system of equations (2) above, the matrices $F(x)$ for new infection terms and $V(x)$ for the other transition terms are defined as follows:

$$F(x) = \begin{pmatrix} \beta\lambda S \\ (1-\beta)\lambda S \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad (3) \text{ and}$$

$$V(x) = \begin{pmatrix} (\varepsilon + \mu + \delta_1 + \theta)A \\ -\varepsilon A - \rho T + (\mu + \delta_2 + \eta + \sigma)C \\ -\eta C + (\mu + \gamma + \delta_3 + \rho)T \\ -\pi - \omega R + (\mu + \lambda)S \\ -\gamma T - \theta A - \sigma C + (\mu + \omega)R \end{pmatrix}. \quad (4)$$

Calculating the partial derivatives of (3) at disease free state N_0 and bearing in the mind that the system (1) has three infected classes, namely, A, C and T we obtain

$$F = \begin{pmatrix} \beta\alpha_1 & \beta\alpha_2 & 0 \\ (1-\beta)\alpha_1 & (1-\beta)\alpha_1 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

In the same manner, partial derivatives of (4) with respect to A, C and T at disease free state N_0 gives $V = \begin{pmatrix} k_1 & 0 & 0 \\ -\varepsilon & k_2 & -\rho \\ 0 & -\eta & k_3 \end{pmatrix}$ and its inverse becomes

$$V^{-1} = \begin{pmatrix} \frac{1}{k_1} & 0 & 0 \\ \frac{\varepsilon k_3}{k_1(k_2k_3+\rho\eta)} & \frac{k_3}{k_2k_3+\rho\eta} & \frac{\rho}{k_2k_3+\rho\eta} \\ \frac{\varepsilon\eta}{k_1(k_2k_3+\rho\eta)} & \frac{\eta}{k_2k_3+\rho\eta} & \frac{k_2}{k_2k_3+\rho\eta} \end{pmatrix}$$

As defined in (Driessche & Watmough, 2002), R_0 is the spectral radius of the next generation matrix, FV^{-1} and it is given by

$$FV^{-1} = \begin{pmatrix} \frac{\beta\alpha_1(k_2k_3+\rho\eta) + \beta\alpha_1\varepsilon k_1k_3}{k_1(k_2k_3+\rho\eta)} & \frac{\beta\alpha_2k_3}{k_2k_3+\rho\eta} & \frac{\beta\rho\alpha_2}{k_2k_3+\rho\eta} \\ \frac{(1-\beta)[\alpha_1(k_2k_3+\rho\eta) + \alpha_2\varepsilon k_1k_3]}{k_1(k_2k_3+\rho\eta)} & \frac{(1-\beta)\alpha_2k_3}{k_2k_3+\rho\eta} & \frac{(1-\beta)\alpha_2\rho}{k_2k_3+\rho\eta} \\ 0 & 0 & 0 \end{pmatrix}.$$

Hence, R_0 of the model (2) can be determined by

$$R_0 = \frac{(1-\beta)\alpha_2k_1k_3 + \beta[k_3(\alpha_1k_2 + \varepsilon\alpha_2) - \alpha_1\rho\eta]}{k_1(k_2k_3+\rho\eta)} \quad \ldots(5)$$

Theorem 3.4. The disease free state is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof. To prove the theorem, we first construct a Jacobian matrix for the system (1) at disease free state

$$J_{N_0} = \begin{pmatrix} -\mu & \alpha_1 & \alpha_2 & 0 & \omega \\ 0 & \beta\alpha_1 - k_1 & \beta\alpha_2 & 0 & 0 \\ 0 & \varepsilon + (1-\beta)\alpha_1 & (1-\beta)\alpha_2 - k_2 & \rho & 0 \\ 0 & 0 & \eta & k_3 & 0 \\ 0 & -\theta & \sigma & \gamma & -(\mu+\omega) \end{pmatrix}. \quad (6)$$

Now we evaluate the Jacobian matrix at DFE and examine its stability effect due to $R_0 > 1$. From the Jacobian matrix (6), we get a characteristic polynomial by computing $det(\lambda I - J_{N_0}) = 0$ as follows:

Stability of disease free state

Local stability of disease free state

$$\begin{vmatrix} \mu+\lambda & \alpha_1 & \alpha_2 & 0 & -\omega \\ 0 & \lambda-(\beta\alpha_1-k_1) & -\beta\alpha_2 & 0 & 0 \\ 0 & -(\varepsilon+(1-\beta)\alpha_1) & (1-\beta)\alpha_2-k_2 & \rho & 0 \\ 0 & 0 & \eta & k_3 & 0 \\ 0 & -\theta & \sigma & \gamma & -(\mu+\omega) \end{vmatrix} = 0,$$

It is obvious that $\lambda_1 = -\mu, \lambda_5 = -(\mu + \omega)$ are two negative eigenvalues of J_{N_0} from the following block matrix:

$$R_{J_{N_0}} = \begin{pmatrix} \lambda-K_1 & -\beta\alpha_2 & 0 \\ -(\varepsilon+(1-\beta)\alpha_1) & \lambda-K_2 & 0 \\ 0 & -\eta & \lambda-K_1 \end{pmatrix},$$

where $K_1 = \beta\alpha_1 - k_1$ and $K_2 = \alpha_2(1-\beta) - k_2$. The characteristic polynomial of $R_{J_{N_0}}$ is given by $P(\lambda) = \lambda^3 + A_1\lambda^2 + A_2\lambda + A_3$ where

$$A_1 = k_3 - K_2 - k_1, A_2 = \beta^2\alpha_1\alpha_2 + K_1K_2 - (\beta\alpha_2\varepsilon + \beta\alpha_1\alpha_2 + K_1k_3 + K_2k_3 + \rho\eta)$$

and

$$A_3 = K_1(K_2k_3 + \rho\eta) + k_3(\beta^2\alpha_1\alpha_2 - \beta\alpha_2\varepsilon - \beta\alpha_1\alpha_2).$$

By applying the Routh-Hurwitz stability criterion (Allen, 2007) and performing some algebraic manipulations, it can be demonstrated that the eigenvalues of the block matrix $R_{J_{N_0}}$ have negative real parts $\Re(\lambda_2), \Re(\lambda_3), \Re(\lambda_4) < 0$, when $R_0 < 1$. Conversely, if $R_0 > 1$, then $A_2 < 0$, indicating that the matrix $R_{J_{N_0}}$ has at least one eigenvalue with a positive real part. Therefore, the DFE point of model (1) is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$.

Global stability of disease free state

This sub-section examines the global stability of the disease-free state.

Theorem 3.5. If $R_0 < 1$, the disease-free state N_0 of model (1) is globally asymptotically stable within its feasible region.

Proof. We start rewriting model (1) as follows: $\frac{dX}{dt} = F(X,Y)$, $\frac{dY}{dt} = G(X,Y)$, with $G(X,0) = 0$ where $X = (S,R) \in R^2$ shows the non-disease classes and $Y = (A,C,T) \in R^3$ shows the disease classes. Two conditions, H_1 and H_2, are necessary for the global asymptotic stability of the DFE of model (1). (H_1) For $\frac{dX}{dt} = F(X,0)$, the point X^* is globally asymptotically stable, where $F(X^*,0) = 0$. (H_2) We have $G(X,Y) = BY - \tilde{G}(X,Y), \tilde{G}(X,Y) > 0$, for $(X,Y) \in \Omega$, where $B = D_Y G(X^*, 0)$ is an M-matrix. The off-diagonal elements of B are non-negative, defining the biologically feasible region in Ω. For model (1), we have:

$$\frac{dX}{dt} = \begin{pmatrix} \pi - \mu S \\ 0 \end{pmatrix}. \quad (7)$$

In fact, the system in (7) above is globally asymptotically stable around $X^* = \left(\frac{\pi}{\mu}, 0\right)$. This can be confirmed by the solution $S(t) = \frac{\pi}{\mu} + (S(0) - \frac{\pi}{\mu})e^{-\mu t}$, which shows that $\lim_{t\to\infty} S(t) = \frac{\pi}{\mu}$. This indicates the global convergence of (7) in Ω. Furthermore, from model (1), we get:

$$B = \begin{pmatrix} \beta\alpha_1 & \beta\alpha_2 & 0 \\ \varepsilon+(1-\beta)\alpha_1 & (1-\beta)\alpha_2-k_2 & \rho \\ 0 & \eta & -k_3 \end{pmatrix}$$

and

$$\tilde{G}(X,Y) = \begin{pmatrix} (\alpha_1 A + \alpha_2 C)\left(\frac{A+C+T+R}{S+A+C+T+R}\right) \\ 0 \\ 0 \end{pmatrix}.$$

Clearly, $\frac{A+C+T+R}{S+A+C+T+R} \geq 0$ inside Ω and therefore, $\tilde{G}(X,Y) \geq 0$. Thus, the two conditions (H_1), and (H_2) satisfied. Hence, the DFE point N_0 of model (1) is globally asymptotically stable when $R_0 < 1$.

Sensitivity analysis

This sub-section discusses the influence of various model parameters on the reproduction number R_0 to understand their comparative effects on disease spread within the community. To conduct the sensitivity analysis, we need to compute the partial derivatives of R_0 with respect to the model parameters. The sensitivity indices related to a parameter p are represented by the normalized forward sensitivity index, which indicates the importance of the parameter in terms of disease transmission and prevalence. Following the methodology outlined in (Chitnis et al., 2008), the normalized forward sensitivity index of the variable R_0, which depends differentiable on the parameter p, is given by:

$$\Psi_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{\partial p}{\partial R_0}.$$

From an explicit formula R_0 in equation (5), we obtain a mathematical expression that calculates the normalized sensitivity indices of R_0 with respect to various parameters that affect R_0. For instance, $\Psi_{\alpha_1}^{R_0} = \frac{\partial R_0}{\partial \alpha_1} \times \frac{\partial \alpha_1}{\partial R_0} = 0.65$. Likewise, we can determine the sensitivity indices for the remaining parameters. The sensitivity indices evaluated at the baseline parameters given in table 2.

Table 2: Sensitivity indices for model parameters.

Parameters	Sensitivity index	Parameters	Sensitivity index
α_1	+ve	μ	-ve
α_2	+ve	ω	-ve
σ	-ve	ρ	-ve
γ	-ve	δ_1	-ve
β	+ve	δ_2	-ve
θ	-ve	δ_3	-ve
ε	+ve	η	-ve

According to table 2 above, if a parameter has a positive sensitivity index, it means that increasing its value will have a significant impact on the frequency of disease spread. For instance, based on the value of $\Psi_{\alpha_1}^{R_0} = 0.65$, we can observe that a 6.5% increase or decrease in the contact rate β will result in a 6.5% increase or decrease in R_0. On the other hand, parameters with negative indices implies that increasing the significance of these parameters would contribute to reducing the severity of the disease.

Table 3: Parameter values of model (1).

Parameters	Value ($\mathbf{year^{-1}}$)	Source	Parameters	Value ($\mathbf{year^{-1}}$)	Source
π	100	Wameko, 2019	σ	0.002	Shi, R., & Cui, Y., 2016
μ	0.0004	Wameko, 2019	θ	0.23	Ainea et al., 2012
β	0.65	Wameko, 2019	γ	0.13	Okosun et al., 2014
δ_1	0.03	Wameko, 2019	ω	0.05	Ainea et al., 2012
δ_2	0.05	Wameko, 2019	ρ	0.05	Teklu et al., 2025
δ_3	0.001	Assumed	α_1	0.002	Wameko, 2019
ε	0.05	Ainea et al., 2012	α_2	0.001	Wameko, 2019

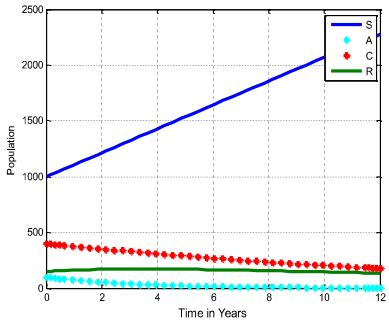

Figure 2. Solution behavior of the HCV model (1) in the absence of treatment.

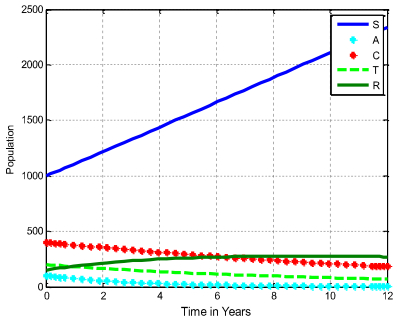

Figure 3. Solution behavior of the HCV model (1) under treatment.

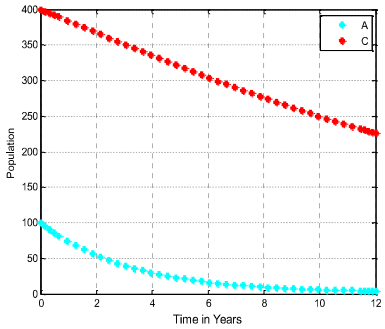

Figure 4. Dynamics of acutely and chronically infected individuals in the absence of treatment.

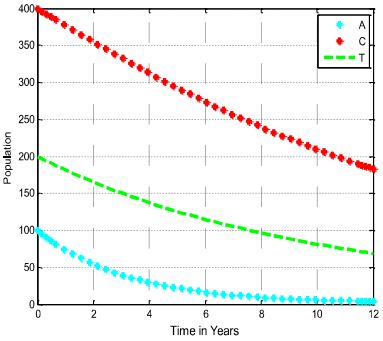

Figure 5. Dynamics of acutely and chronically infected individuals under treatment.

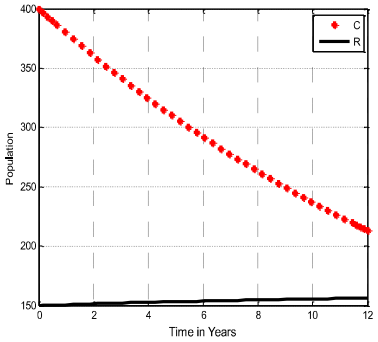

Figure 6. Dynamics of chronically infected and recovered individuals in the absence of treatment.

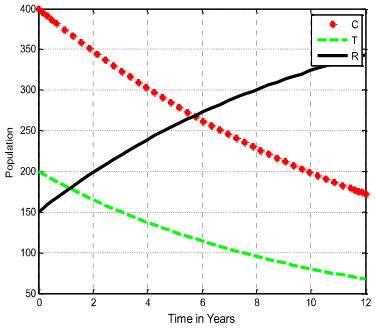

Figure 7. Dynamics of chronically infected and recovered individuals under treatment.

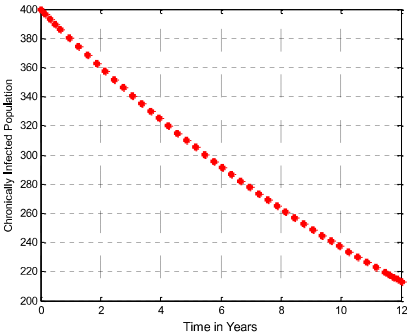

Figure 8. Dynamics of chronically infected individuals in the absence of treatment

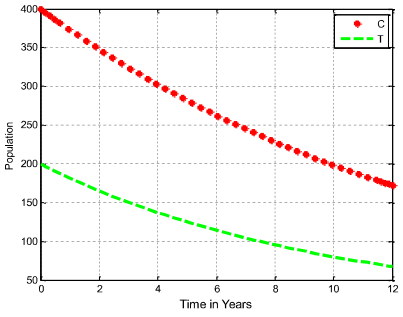

Figure 9. Dynamics of chronically infected treatment

Discussion

This segment aims to explain the simulation results and highlight their implications for the state variables and parameter values. In the absence of treatment, the numerical simulation in Fig. 2 demonstrates a gradual decline in both chronically infected and recovered individuals, with the model solutions converging to an HCV endemic equilibrium after around twelve years. Conversely, Fig. 3 illustrates that, with treatment, the population of chronically infected individuals' decreases while the population of recovered individuals gradually increases over time. A comparison of Figs. 4 and 5 reveals the impact of treatment on acutely and chronically infected individuals. While the acutely infected population decreases similarly in both figures (as treatment is not applied to acute cases), the chronically infected population differs significantly. Without treatment (Fig. 4), this population remains above 200, while treatment (Fig. 5) reduces it below 200. Figs. 6 and 7 illustrate the dynamics of chronically infected and recovered individuals without and with treatment, respectively. In Fig. 6, chronic infections decrease gradually while recovery shows minimal increase. However, Fig. 7 reveals that treatment leads to a more pronounced decline in chronic infections and a rapid increase in recovered individuals. The impact of treatment on chronically infected individuals is evident in Figs. 8 and 9. Fig. 8 illustrates the dynamics of chronically infected individuals in the absence of treatment, while Fig. 9 shows the same dynamics with treatment. The decline in chronically infected persons is significantly faster in Fig. 9 due to the treatment's effects. The timely identification and treatment of chronically infected individuals, employing either direct-acting antivirals (DAAs) or natural herbal supplements with physician consultation, holds promise for effectively eliminating HCV within a shorter time frame.

Conclusion

In this research article, we derived and analyzed a deterministic mathematical model of HCV using a system of first-order non-linear differential equations. Our model uses five non-linear ordinary differential equations to describe the interactions between susceptible, acutely infected, chronically infected, treated, and recovered individuals. The model aims to reduce the number of acute and chronic cases, and it specifically considers treatment for individuals with chronic infection. In this study, we first established basic analytical properties, including positivity, boundedness of solutions, and identification of disease-free and endemic equilibrium points. Subsequently, we investigated the basic reproduction number and proved the local and global stability of the disease-free equilibrium point. We conducted numerical simulations using MATLAB software to validate our theoretical findings and illustrate the impact of treatment on HCV viral dynamics. The numerical simulations closely aligned with our theoretical predictions. The results demonstrated that early identification and treatment of chronically infected individuals accelerates HCV elimination by reducing chronic infections and increasing recovery rates. Future research will refine the model by incorporating optimal control measures to optimize disease management strategies, validating it with real-world population data, and analyzing cost-benefit ratios, resource availability, population demographics, and local healthcare infrastructure.

Data availability

All data were incorporated in the manuscript.

Declaration of competing interest

The writers approve there are no well-known competing financial benefits or individual affairs that could be seen as influencing the work offered in this article.

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