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Global analysis of a mathematical model for Hepatitis C virus transmissions

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ABSTRACT

In this paper, a mathematical model is proposed and analyzed for Hepatitis C virus (HCV) infection transmissions. In this model, both of chronic primary infection and possibility of reinfection are considered. Two thresholds of basic reproduction number R_0 and control reproduction number R_c are derived. We get the sufficient conditions for the existence of infection-free equilibrium and endemic equilibrium. The sufficient conditions for the local and global stability of the equilibria are also obtained. Some numerical simulations are performed to prove the theoretical results. At last, some discussions are presented.

1. Introduction

The Hepatitis C virus (HCV) is an RNA virus that belongs to the family flaviviridae which replicates in the cytoplasm of hepatocytes but is not directly cytopathic (Chen and Morgan, 2006). HCV, first discovered in 1989, has now become a serious public health issue. It is reported that more than 170 million people have been affected worldwide. After exposure to HCV, approximately 85% of the patients developed to chronic infection, and then some of these patients progressed to cirrhosis and hepatocellular carcinoma, until death (Seeff and Hoofnagle, 2003). About 30% of all liver transplants in industrialized countries are a result of end stage HCV induced liver disease, presenting a significant burden on health care costs (Seeff and Hoofnagle, 2003). Nowadays, there is still no vaccine and no post-exposure prophylaxis for HCV. However, seven genotypes and 67 subtypes of HCV have been found around the world (Smith et al., 2014). It is disappointing that current standard therapy, involving pegylated interferon and ribavirin, is effective in only approximately 40% of the patients, who are infected with the highly prevalent genotype 1 (Ghany et al., 2009; Manns et al., 2001).

The most frequently cited factors accounting for the bulk of HCV transmission worldwide are injection drug use, blood transfusions from unscreened donors, unsafe therapeutic injections, and other health-care-related procedures. Evidence accumulated by most developed countries indicated that the predominant source of new HCV infections over the past few decades is injection drug use. Unsafe therapeutic injections and transfusions are the major modes of transmission in the developing countries, especially in countries where age-specific seroprevalence rates suggest ongoing increased risk of HCV infection (Wasley and Alter, 2000). In developed countries with high seroprevalence in older age groups, unsafe therapeutic injections probably had a substantial role in HCV transmission 30–50 years ago, and may persist as an important cause of transmission in isolated, hyperendemic areas (Zeiler et al., 2010; Guadagnino et al., 1997; Okayama et al., 2002).

Treatment strategies for HCV in cell level(micro level) are discussed by many researchers, such as (Carnero and Fortes, 2016; Uchida et al., 2016; Wang et al., 2015). However, some other scientists tried to use mathematical models to study HCV in population level (macro level). For example, mathematical model for HCV RNA kinetics were developed to assess the viral dynamics in vivo and the antiviral efficacy of therapy (Rong and Perelson, 2010; Neumann et al., 1998). A compartmental model for diseases with carrier states is considered and susceptible individuals can be infected by either carriers or acutely infectious individuals in the model (Keeling and Rohani, 2008). Besides, Yuan and Yang proposed an SEIV model with acute and chronic stages, which was similar to the transmission of HCV, but they did not take the recovery from the acute

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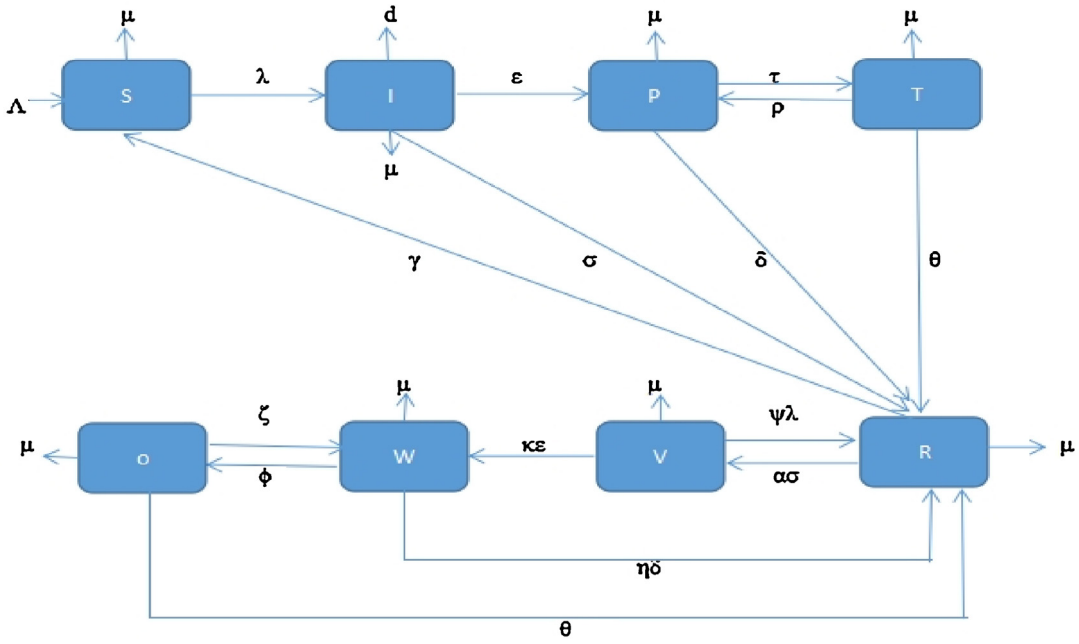

Fig. 1. Transfer diagram of the HCV infection transmission model with treatment. The model divides the population into 8 major groups according to their susceptibilities and infectiousness.

infected stage into consideration (Yuan and Yang, 2008). An SIR model is used to study the transmission of HCV among injecting drug users (Kretzschmar and Wiessing, 2004). But, none of these models consider directly reinfection. Reinfections following recovery behave differently from primary infections. For example, the spontaneous viral clearance rate in reinfected patients is higher compared with that in primary infected patients (Osburn et al., 2010). Also, viral load during episodes of reinfection is significantly lower than that of the primary infection in the same subjects, suggesting lower infectiousness of reinfections (Bate et al., 2010; Grebely et al., 2006; Mehta et al., 2002).

In order to increase our understanding of HCV disease, we construct a mathematical model for HCV transmission with the objective of assessing the potential public health impact of therapy to help us to gain insights into the disease transmission, and assess the effectiveness of preventive strategies and then control of it eventually (Zhang and Zhou, 2012). Though our model is similar to Elbasha (2013), but they had not consider the factor of death due to disease, and the numerical simulations are very different.

The paper is organized as follows. In Section 2, we introduce some assumptions and propose the model. In Section 3, qualitative analysis of the model is presented. In Section 4, some numerical simulations are provided to verify the theoretical results. And in the last section, some conclusions and discussions are provided.

2. Model formulation

In our model reinfection is considered. The total number of population is divided into eight classes: susceptible to infection (S), acutely infected (I), persistently (chronically) infected (P), removed (R), acute reinfection (V), chronic reinfection (W), treatment for chronical infection (T), and treatment for chronical reinfection (Q). (Fig. 1)

To formulate the model we make the following assumptions:

(H1) The rate of recruitment in the naive class S is Λ, and natural death rate for all classes is μ. The death rate due to acute infection and acute reinfection is d.

(H2) Susceptible individuals are infected at a per capita rate λ that depends on the contact rate β and the patterns of interaction between persons. The residual susceptibility of persons in class R is measured by ψ such that the force of infection is $\psi\lambda$ and $\psi \leq 1$. The rate of progression to chronic stage of primary host and reinfection host is ε and κ, respectively.

(H3) A primary infected host can clear acute infection at rate σ and chronic infection at rate δ. A reinfected host can clear acute infection at rate $\alpha\sigma$ ($\alpha \geq 1$ is a constant) and chronic infection at rate $\eta\delta$ ($\eta \geq 1$ is a constant). Immunity of persons in compartment R wanes and eventually they return to the susceptible class S at rate γ.

(H4) Since the period of acute infection is short, we only provide treatment to the chronically infected individuals and chronically reinfected individuals. The treatment rate of chronically infected population and chronically reinfected population is τ and ϕ, respectively. After the treatment, a fraction of patients succeed in clearing HCV, and move to class R at rate θ. The remainder fail to treatment and move back to class P at rate ρ and class W at rate ζ.

(H5) The degree of infectiousness of hosts in classes P, V, W, T and Q relative to that of hosts in class I is π, ν, $\omega\pi$, $\chi\pi$ and $\chi\pi$, respectively.

According to the above assumptions, we establish the system as

$$\begin{cases} S' = \Lambda - \lambda S - \mu S + \gamma R, \\ I' = \lambda S - (\mu + \sigma + \varepsilon + d)I, \\ P' = \varepsilon I + \rho T - (\mu + \delta + \tau)P, \\ R' = \sigma I + \delta P + \alpha\sigma V + \eta\delta W + \theta T + \theta Q - \psi\lambda R - (\mu + \gamma)R, \\ V' = \psi\lambda R - (\mu + \alpha\sigma + \kappa\varepsilon + d)V, \\ W' = \kappa\varepsilon V + \zeta Q - (\mu + \eta\delta + \phi)W, \\ T' = \tau P - (\mu + \rho + \theta)T, \\ Q' = \phi W - (\mu + \zeta + \theta)Q, \end{cases} \tag{1}$$