

based on the clinical information of past patients. Aghajanzadeh et al. [23] suggested an adaptive control strategy for hepatitis B virus infection inside the human body by antiviral drugs. They considered model parameters uncertainties on model parameters and employed adaptive controller to control the dynamic despite uncertainties of the system. Sharifi and Moradi [24] designed a robust scheme with adaptive gains to control the influenza epidemic, considering its dynamic model's uncertainties. Padmanabhan et al. [25] proposed an optimal adaptive method to control the sedative drug in anesthesia administration. They employed an integral reinforcement learning method in order to overcome the uncertainty of parameter values.

3. DYNAMIC MODEL OF HEPATITIS C VIRUS EPIDEMIC

Mathematical modeling is a useful way of analyzing the epidemiology of a disease. These models have two important capabilities: (1) finding out mechanistic understanding of the disease and (2) exploring potential outcomes of the epidemic under different conditions [26]. For assessment of the proposed method for the HCV prevalence control in a population, a nonlinear compartmental model is used with five different classes including unaware susceptible (S_u), aware susceptible (S_a), acutely infected (I), chronically infected (C), and the treated (T) humans [4]. The susceptible compartment is divided into two classes, including aware and unaware people. Note that aware people have information about the HCV transmission ways and preventing methods despite the unaware population. Since there is no available vaccine for the HCV, informing people about preventing methods is a very important way to reduce the risk of infection for susceptible people [1]. Therefore, the unaware susceptible individuals (S_u) will be infected in contact with the infected population (I , C , and T) with a higher rate in comparison with the aware susceptible individuals (S_a) [4]. Thus, the transmission rate for unaware susceptible humans (S_u) should be considered larger than this rate for aware susceptible humans (S_a) in the dynamic model [4]. The nonlinear mathematical model of HCV epidemic is as follows:

$$\begin{aligned}
 \dot{S}_u &= b - \lambda_{S_u} \frac{S_u}{N} - (\mu + u_1(t))S_u + (1-q)\gamma I \\
 \dot{S}_a &= u_1(t)S_u - \lambda_{S_a} \frac{S_a}{N} - \mu S_a + (1-p)\xi T \\
 \dot{I} &= \lambda_{S_u} \frac{S_u}{N} + \lambda_{S_a} \frac{S_a}{N} - (\mu + \gamma)I \\
 \dot{C} &= q\gamma I - (\mu + u_2(t) + \theta)C + p\xi T \\
 \dot{T} &= u_2(t)C - (\mu + \xi)T
 \end{aligned} \tag{1}$$

where $\lambda_{S_u} = \beta(I + K_1 C + K_2 T)$ and $\lambda_{S_a} = \alpha \lambda_{S_u}$. u_1 and u_2 are control inputs and defined respectively as the effort rate to inform unaware susceptible individuals and the treatment rate for chronically infected class. N denotes the total population and will be calculated as

$$N = S_u + S_a + I + C + T \tag{2}$$

The population of unaware susceptible (S_u) increases with the rate of b . Unaware and aware susceptible individuals are also infected in contact with acutely and chronically infected and treated individuals at the rates of λ_{S_u} and λ_{S_a} , respectively. Infectiousness rate for acutely infected people is higher than chronically infected individuals, and the treated people have the lowest rate; thus, it is assumed that $K_1 > K_2$ [4, 5]. The total population (N) decreases with two different rates μ and θ , where μ denotes the rate of natural death that decreases populations of all compartments. However, θ is the rate of HCV-induced death and decreases the population of the chronically infected compartment (C).

During the acute stage (I), the HCV could have different behaviors for each patient based on his/her immune system response. For 15%–25% of cases in this stage, the RNA of HCV becomes indistinguishable in their blood serum and the ALT level returns to the normal range. This observation is defined by the term $(1-q)\gamma I$ in the proposed HCV dynamics [4, 6]. Approximately, the immune system in 75%–85% of the patients could not remove the hepatitis C virus in the acute stage and their disease becomes advanced to the chronic stage. Note that if the HCV RNA remains in the patient's blood for at least 6 months after the onset of acute infection, the chronic level of the disease will appear which is defined by the term $q\gamma I$ in Eq. (1) [5, 6]. Finally, the defeat in the treatment process is defined by the term p . The treated population decreases by the rate of ξT and joins the chronic class by the rate of $p\xi T$ in the case of treatment failure and the rest of this population $(1-p)\xi T$ will join the aware susceptible class if the treatment is successful. The schematic diagram of the proposed nonlinear dynamics of the HCV epidemic is depicted in Fig. 1 and descriptions of the parameters are presented in Table 1 [4].

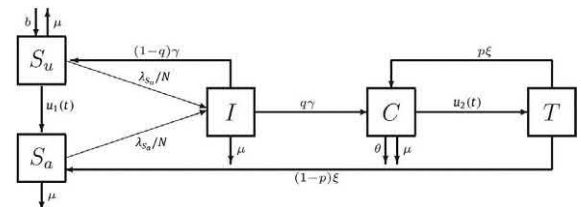


FIG. 1 Schematic diagram of population transmission among different classes of HCV epidemic.