

## ASYMPTOTIC BEHAVIOR OF DIFFERENT CONTROLS OF HEPATITIS B VIRUS

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**ABSTRACT.** In this paper, we introduce a hepatitis B virus stochastic transition model with vaccination and awareness campaign. The purpose of this work is to show the effect of vaccine and awareness in the affected area of hepatitis B. For this purpose first, we formulate the stochastic model for hepatitis B virus, then investigate the asymptotic behavior of vaccination and awareness campaign, through the unique positive solution of our proposed model. We study the different scenarios in order to identify the best control of this virus. Graphical justification is also presented.

**Key Words:** Hepatitis B virus; stochastic modeling; unique positive solution; stability analysis

**Subject, Classification:** 92D25, 49J15, 93D20, 91G20.

### 1. PRELIMINARIES

A hepatitis B virus (HBV) infection is a global health disease which transmits through unhealthy food as well as by their carriers. According to the analysis of World Health Organization about 2000 millions people have been infected with this virus and about 350 millions, among them, are its carriers [1]. There appear about 4 million acute clinical cases and 25 percent of its carriers each year. Moreover about 1 million die, due to this virus, each year. For the control of HBV mathematicians also play an important rule in the sense of making different models to study the dynamical behavior of this virus.

Jinhua Pang et al. [1] and Zou et al. [2] in 2009 considered a deterministic HBV transmission model with vaccination, where vaccination took place in China to all newborns. They have shown that, with regular vaccination to newborns, the number of children having HBV infection as well as the number of carriers decreased dramatically. Anderson and May 1991 [5] have discussed the effects of carriers on the transmission of this virus by using a simple mathematical model. Zhao et al. 2000 [3] presented an age structure model to study the long-term effect of vaccination on the

HBV transmission in China. Wang et al. 2008 [4] studied HBV infection in a diffusion model restricted to a finite domain. Similarly Xu and Ma 2009 [6] proposed an HBV model with spatial diffusion respond in the infection rate. Different authors studied the models describing the HBV as well as stochastic models [7, 8, 9, 10, 11, 12, 13].

In this work, we extend the deterministic model of Jinhua Pang et al. [1] to a stochastic HBV transmission model with addition of migrated class and vaccination plus awareness campaign to all latent ones. First, we study the stability of the corresponding deterministic model and then discuss the asymptotic number of acute, carriers and immunity classes, in the case when the number of susceptible and latent's increases/decreases as linear, through the unique positive solution of our stochastic model under different scenarios in order to identify the expected optimal control of HBV.

The rest of the paper is organized as: in Section 2, we give the formulation of model and discuss the stability of stochastic model. In Section 3, we apply different controls and discuss the different scenarios with the obtained figures through Matlab. Finally, we give conclusion in Section 4.

## 2. Notations and Formulation of the Model

We propose a stochastic transition HBV model with vaccination to acute as well as latent ones. We divide the total population in five classes: the Susceptible  $S = (S(t))$ , Latent  $L = (L(t))$ , Acute ones  $A = (A(t))$ , HBV Carriers  $C = (C(t))$  and temporary protective Immunity  $I = (I(t))$  at time  $t \geq 0$ .

We assume that all the parameters of the model are non-negative and denote by  $\lambda$  the recruitment rate such that  $\lambda m$ ,  $0 \leq m \leq 1$ , number of individuals adds to susceptible while  $\lambda(1 - m)$  flow to latent ones,  $d_i, i = 1, 2, \dots, 5$ , denote the death rate of  $S, L, A, C$  and  $I$  respectively,  $\mu$  is the child birth rate,  $\omega$  is the rate of failure immunization,  $\beta$  is the transmission coefficient,  $\sigma$  is the rate at which latent individuals becoming infections,  $n$  ratio of latent moves to immunity class due to vaccination and,  $\delta$  is the rate of loss of immunity class,  $r_1$  is the rate at which an individual leaves class  $A$ , carriers recover with the rate  $r_2$ , the infectiousness rate of carriers relative to acute infection is  $\alpha$ ,  $q$  ( $0 \leq q \leq 1$ ) is the rate at which acute infection individuals become carrier while  $1 - q$  is the rate at which acute infection individuals clear HBV and move to immunity class. Moreover new born are vaccinated immediately after his/her birth and  $\mu(1 - w)$  part of them move to immunity class.

We introduce stochastic components on the transition rates, that is, on the transition from  $S$  to  $L$  with drift term  $\beta(A + \alpha C)$  and variance  $\sigma_1$ ,  $L$  to  $A$  with drift  $\sigma$  and volatility  $\sigma_2$ ,  $A$  to  $C$  with drift  $qr_1$  with volatility  $\sigma_3$ ,  $C$  to  $I$  with drift  $r_2$  and volatility  $\sigma_4$  and  $I$  to  $S$  with drift  $\delta$  and volatility  $\sigma_5$ .

We consider a probability space  $(\Omega, \mathcal{F}, P)$  and a five dimensional Wiener process  $W = (W_1(t), W_2(t), \dots, W_5(t))$  on it, where each  $W_i(t), i = 1, 2, \dots, 5$  is a standard Wiener process, independent of each other, with mean zero and variance  $t$  at time  $t$ . Denote by  $\mathcal{F}^W = (\mathcal{F}^{W(t)})_{t \geq 0}$  the augmentation of the natural filtration of the Wiener processes by  $P$ -null sets of  $\mathcal{F}$ . On the filtered probability space  $(W, \mathcal{F}, \mathcal{F}^{W(t)}, P)$  we will consider five random functions  $S(t), L(t), A(t), C(t)$  and  $I(t)$ .

Evolution of these functions obey the following system of stochastic differential equations

$$\begin{aligned}
(2.1) \quad dS(t) &= [\lambda m + \mu\omega(1 - \epsilon C(t)) - \{\beta(A(t) + \alpha C(t)) \\
&\quad + p(1 - \omega) + d_1 - \delta I(t)\}S(t)]dt \\
&\quad - \sigma_1(A(t) + \alpha C(t))S(t)dW_1(t) + \sigma_5 S(t)I(t)dW_5(t), \\
(2.2) \quad dL(t) &= (\lambda(1 - m) + \mu\omega\epsilon C(t) + \beta(A(t) + \alpha C(t))S(t) - (n + \sigma + d_2)L(t))dt \\
&\quad + \sigma_1(A(t) + \alpha C(t))S(t)dW_1(t) - \sigma_2 L(t)dW_2(t), \\
(2.3) \quad dA(t) &= (\sigma L(t) - (d_3 + r_1)A(t))dt + \sigma_2 L(t)dW_2(t) - \sigma_3 q A(t)dW_3(t), \\
(2.4) \quad dC(t) &= (qr_1 A(t) - (d_4 + r_2)C(t))dt + \sigma_3 q A(t)dW_3(t) - \sigma_4 C(t)dW_4(t), \\
(2.5) \quad dI(t) &= (r_2 C(t) + \mu(1 - \omega) + (1 - q)r_1 A(t) + nL(t) \\
&\quad + p(1 - \omega)S(t) - (d_5 + \delta)I(t))dt \\
&\quad + \sigma_4 C(t)dW_4(t) - \sigma_5 I(t)dW_5(t),
\end{aligned}$$

where we have assumed that all the coefficients in the model are Lipschitz continuous.

From the above system, the dynamics of  $S(t)$  can be described by:

$$\begin{aligned}
(2.6) \quad S(t) &= e^{-(p(1-\omega)+d_1)t - \int_0^t (\beta(A(u)+\alpha C(u))+\alpha C(u)-\delta I(u))du} \\
&\quad - \frac{\sigma_1^2}{2} \int_0^t (A(u) + \alpha C(u))^2 du - \frac{\sigma_5^2}{2} \int_0^t I(u)^2 du \\
&\quad \times e^{-\sigma_1 \int_0^t (A(u)+\alpha C(u))dW_1(u) + \sigma_5 \int_0^t I(u)dW_5(u)} \left[ S(0) - \mu\omega\epsilon \int_0^t C(u)e^{(p(1-\omega)+d_1)u} \right. \\
&\quad \times e^{\int_0^u (\beta(A(v)+\alpha C(v))+\alpha C(v)-\delta I(v))dv + \frac{\sigma_1^2}{2} \int_0^u (A(v)+\alpha C(v))^2 dv + \frac{\sigma_5^2}{2} \int_0^u I(v)^2 dv} \\
&\quad \left. \times e^{\sigma_1 \int_0^u (A(v)+\alpha C(v))dW_1(v) - \sigma_5 \int_0^u I(v)dW_5(v)} du \right] \\
&\quad + (\lambda m + \mu\omega) \int_0^t e^{-(p(1-\omega)+d_1)(t-u) - \int_u^t (\beta(A(v)+\alpha C(v))+\alpha C(v)-\delta I(u))du} \\
&\quad - \frac{\sigma_1^2}{2} \int_u^t (A(v) + \alpha C(v))^2 du \\
&\quad \times e^{-\frac{\sigma_1^2}{2} \int_u^t I(v)^2 dv - \sigma_1 \int_u^t (A(v)+\alpha C(v))dW_1(v) + \sigma_5 \int_u^t I(v)dW_5(v)} du,
\end{aligned}$$

with expected value

(2.7)

$$\begin{aligned} E(S(t)) &= E e^{-(p(1-\omega)+d_1)t - \int_0^t (\beta(A(u)+\alpha C(u))+\alpha C(u)-\delta I(u))du} \left[ S(0) \right. \\ &\quad \left. - \mu\omega\epsilon E \int_0^t C(u) e^{(p(1-\omega)+d_1)u} \times e^{\int_0^u (\beta(A(v)+\alpha C(v))+\alpha C(v)-\delta I(v))dv} \right] \\ &\quad + (\lambda m + \mu\omega) E \int_0^t e^{-(p(1-\omega)+d_1)(t-u) - \int_u^t (\beta(A(u)+\alpha C(u))+\alpha C(u)-\delta I(u))du} du, \end{aligned}$$

where we have used the property of exponential martingales (see, Karatzas and Shreve [14, 15]) like

$$(2.8) \quad E e^{\int_s^t a(u) dW_u - \frac{1}{2} \int_s^t a^2(u) du} = 1,$$

where  $a(t)$  is any  $\mathcal{F}^W(t)$ -measurable function and  $W(t), t \geq 0$ , is any standard Wiener process.

Dynamics of  $L(t)$  is given as

$$\begin{aligned} (2.9) \quad L(t) &= e^{-\left(n+\sigma+d_2+\frac{\sigma_2^2}{2}\right)t - \sigma_2 W_2(t)} \left[ L(0) \right. \\ &\quad \left. + \int_0^t (\mu\omega\epsilon C(u) + \beta(A(u) + \alpha C(u))S(u)) \times e^{\left(n+\sigma+d_2+\frac{\sigma_2^2}{2}\right)u + \sigma_2 W_2(u)} du \right. \\ &\quad \left. + \sigma_1 \int_0^t e^{\left(n+\sigma+d_2+\frac{\sigma_2^2}{2}\right)u + \sigma_2 W_2(u)} (A(u) + \alpha C(u))S(u) dW_1(u) \right] \\ &\quad + \lambda(1-m) \int_0^t e^{-\left(n+\sigma+d_2+\frac{\sigma_2^2}{2}\right)(t-u) - \sigma_2(W_2(t)-W_2(u))} du. \end{aligned}$$

Using properties like (2.8) and of the Itô's integral

$$(2.10) \quad E \int_0^t b(u) dW_u = 0,$$

where  $b(t)$  is some  $\mathcal{F}^W(t)$ -measurable function, we obtain the expected value of  $L(t)$  as

$$\begin{aligned} (2.11) \quad E(L(t)) &= e^{-(n+\sigma+d_2)t} \left[ L(0) \right. \\ &\quad \left. + E \int_0^t (\mu\omega\epsilon C(u) + \beta(A(u) + \alpha C(u))S(u)) e^{(n+\sigma+d_2)u} du \right] \\ &\quad + \frac{\lambda(1-m)}{n+\sigma+d_2} (1 - e^{-(n+\sigma+d_2)t}). \end{aligned}$$

Similarly

$$(2.12) \quad A(t) = e^{-\left(d_3+r_1+\frac{\sigma_3^2 q^2}{2}\right)t-\sigma_3 q W_3(t)} \left[ A(0) + \int_0^t L(u) e^{\left(d_3+r_1+\frac{\sigma_3^2 q^2}{2}\right)u+\sigma_3 q W_3(u)} (\sigma du + \sigma_2 dW_2(u)) \right],$$

with expectation

$$(2.13) \quad E(A(t)) = e^{-(d_3+r_1)t} \left[ A(0) + \sigma E \int_0^t L(u) e^{(d_3+r_1)u} du \right].$$

While

$$(2.14) \quad C(t) = e^{-\left(d_4+r_2+\frac{\sigma_4^2}{2}\right)t-\sigma_4 W_4(t)} \left[ C(0) + q \int_0^t A(u) e^{\left(d_4+r_2+\frac{\sigma_4^2}{2}\right)u+\sigma_4 W_4(u)} (r_1 du + \sigma_3 dW_3(u)) \right],$$

with expected value

$$(2.15) \quad E(C(t)) = e^{-(d_4+r_2)t} \left[ C(0) + q r_1 E \int_0^t A(u) e^{(d_4+r_2)u} du \right].$$

And

$$(2.16) \quad I(t) = e^{-\left(d_5+\delta+\frac{\sigma_5^2}{2}\right)t-\sigma_5 W_5(t)} \left[ I(0) + \int_0^t e^{\left(d_5+\delta+\frac{\sigma_5^2}{2}\right)u+\sigma_5 W_5(u)} \times (\mu(1-\omega) + r_2 C(u) + (1-q)r_1 A(u) + p(1-\omega)S(u) + nL(u)) du + \sigma_4 C(u) dW_4(u) \right],$$

with

$$(2.17) \quad E(I(t)) = e^{-(d_5+\delta)t} \left[ I(0) + \mu(1-\omega) \int_0^t e^{(d_5+\delta)u} du + \int_0^t e^{(d_5+\delta)u} (r_2 C(u) + (1-q)r_1 A(u) + p(1-\omega)S(u) + nL(u)) du \right].$$

Under the assumption  $E(S(t+)|S(t)) = k_1$  and  $E(L(t+)|L(t)) = k_2$ , where  $k_1, k_2 \in R$ , of linear growth/decay, we have

$$(2.18) \quad E(A(t)) = A(0) e^{-(d_3+r_1)t} + \frac{\sigma k_2}{d_3+r_1} (1 - e^{-(d_3+r_1)t}),$$

$$(2.19) \quad E(C(t)) = C(0) e^{-(d_4+r_2)t} + \frac{q r_1 A(0) e^{-(d_4+r_2)t}}{d_4+r_2-d_3-r_1} (e^{(d_4+r_2-d_3-r_1)t} - 1) + \frac{q r_1 \sigma k_2}{(d_3+r_1)(d_4+r_2)} (1 - e^{-(d_4+r_2)t}) - \frac{q r_1 \sigma k_2 e^{-(d_4+r_2)t}}{(d_3+r_1)(d_4+r_2-d_3-r_1)} (e^{(d_4+r_2-d_3-r_1)t} - 1),$$

while

$$\begin{aligned}
(2.20) \quad E(I(t)) &= I(0)e^{-(d_5+\delta)t} + \left[ (1-\omega)(\mu + pk_1) + nk_2 + \frac{\sigma r_1 k_2 (d_4 + r_2 - qd_4)}{(d_3 + r_1)(d_4 + r_2)} \right] \\
&\times \left( \frac{1 - e^{-(d_5+\delta)t}}{d_5 + \delta} \right) + \frac{r_2 C(0) e^{-(d_5+\delta)t}}{d_5 + \delta - d_4 - r_2} (e^{(d_5+\delta-d_4-r_2)t} - 1) \\
&+ \frac{r_1 A(0)(d_4 + r_2 - d_3 - r_1 - q(d_4 - d_3 - r_1)) e^{-(d_5+\delta)t}}{(d_4 + r_2 - d_3 - r_1)(d_5 + \delta - d_3 - r_1)} \\
&(e^{(d_5+\delta-d_3-r_1)t} - 1) \\
&+ qr_1 r_2 e^{-(d_5+\delta)t} \left[ \frac{\sigma k_2}{(d_4 + r_2 - d_3 - r_1)(d_4 + r_2)} - \frac{A(0)}{d_4 + r_2 - d_3 - r_1} \right] \\
&\times \left( \frac{e^{(d_5+\delta-d_4-r_2)t} - 1}{d_5 + \delta - d_4 - r_2} \right) - \sigma k_2 r_1 e^{-(d_5+\delta)t} \left( \frac{e^{(d_5+\delta-d_3-r_1)t} - 1}{d_5 + \delta - d_3 - r_1} \right) \\
&\times \frac{d_4 + r_2 - d_3 - r_1 - q(d_4 - d_3 - r_1)}{(d_3 + r_1)(d_4 + r_2 - d_3 - r_1)}.
\end{aligned}$$

### 3. Scenarios:

1. When  $d_3 + r_1 = 0$  and  $k_2 > 0$ , then the asymptotic behaviour of  $E(A(t))$ ,  $E(C(t))$  and  $E(I(t))$  is as

$$\lim_{t \rightarrow \infty} E(A(t)) = \infty, \lim_{t \rightarrow \infty} E(C(t)) = 0, \lim_{t \rightarrow \infty} E(I(t)) = \frac{1}{d_5 + \delta} ((1 - \omega)(\mu - pk_1) + nk_2),$$

and if  $k_2 < 0$ , then  $E(A(t))$ ,  $E(C(t))$  and  $E(I(t))$  decrease and  $E(A(t))$  vanishes at time  $t = \frac{-A(0)}{\sigma k_2}$ , vanishing time of  $E(C(t))$  and  $E(I(t))$  can be obtained by using expressions (2.15) and (2.17). 2. Similarly when  $d_4 + r_2 = 0$  then

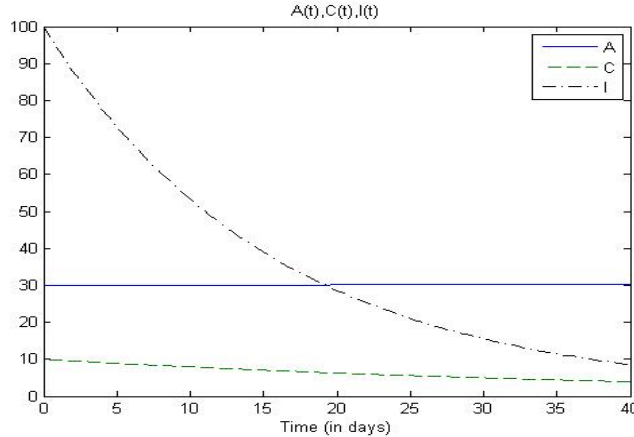


FIGURE 1. With parameters values  $\beta = 0.48$ ,  $m = 0.02$ ,  $d_2 = 0.5$ ,  $\gamma = 0.02$ ,  $d_3 = 0.01$ .

$$\lim_{t \rightarrow \infty} E(A(t)) = \frac{\sigma k_2}{d_3 + r_1}, \lim_{t \rightarrow \infty} E(C(t)) = \infty,$$

$$\lim_{t \rightarrow \infty} E(I(t)) = \frac{1}{d_5 + \delta} ((1 - \omega)(\mu - pk_1) + nk_2) + \frac{(1 - q)r_1\sigma k_2}{(d_3 + r_1)^2}.$$

3. And when  $d_5 + \delta = 0$  then

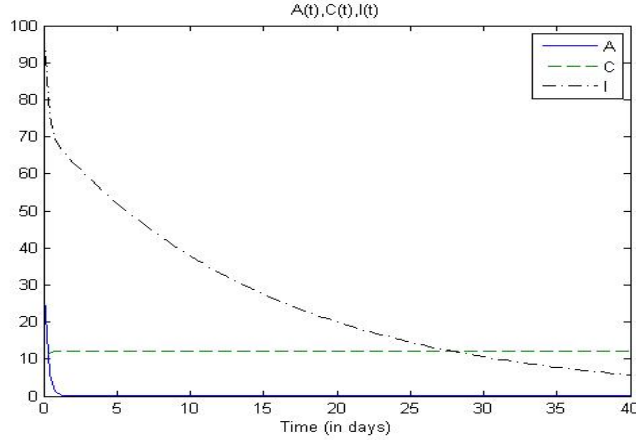


FIGURE 2. With parameters values  $\beta = 0.48, m = 0.02, d_2 = 0.5, \gamma = 0.02, d_3 = 0.01$ .

$$\lim_{t \rightarrow \infty} E(A(t)) = \frac{\sigma k_2}{d_3 + r_1}, \lim_{t \rightarrow \infty} E(C(t)) = \frac{qr_1\sigma k_2}{(d_3 + r_1)(d_4 + r_2)}, \lim_{t \rightarrow \infty} E(I(t)) = \infty.$$

4. Moreover, for positive  $d_4 + r_2, d_3 + r_1,$  and  $d_5 + \delta,$  with arbitrary equality or

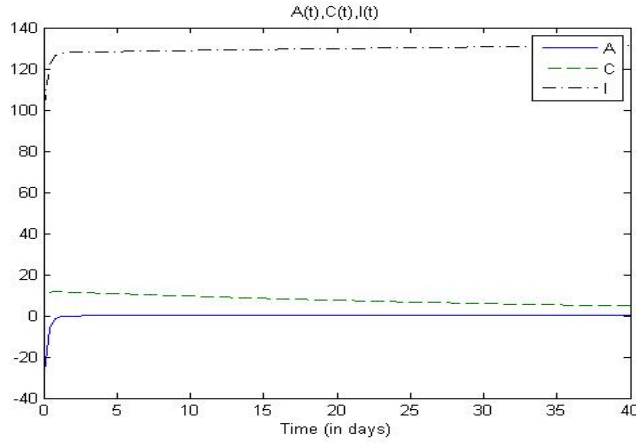


FIGURE 3. With parameters values  $\beta = 0.48, m = 0.02, d_2 = 0.5, \gamma = 0.02, d_3 = 0.01$ .

inequality relation between them, we have the asymptotic stability as

$$\lim_{t \rightarrow \infty} E(A(t)) = \frac{\sigma k_2}{d_3 + r_1}, \lim_{t \rightarrow \infty} E(C(t)) = \frac{qr_1\sigma k_2}{(d_4 + r_2)(d_3 + r_1)},$$

$$\lim_{t \rightarrow \infty} E(I(t)) = \frac{1}{d_5 + \delta} \left[ (1 - \omega)(\mu + pk_1) + nk_2 + \frac{qr_1r_2\sigma k_2}{(d_3 + r_1)(d_4 + r_2)} + \frac{(1 - q)r_1\sigma k_2}{d_3 + r_1} \right].$$

$d_1 = d_2 = d_3 = d_4 = d_5 = \lambda = \mu = \frac{1}{70}, \omega = .05, \sigma = 6, \delta = .05, r_1 = 4, r_2 = .009, \epsilon = .8, q = .07, p = .5, \beta = 5, \alpha = .5, S(0) = 40, L(0) = 20, A(0) = 30, C(0) = 10, I(0) = 100, k_1 = k_2 = .001, \sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = \sigma_5 = .01$

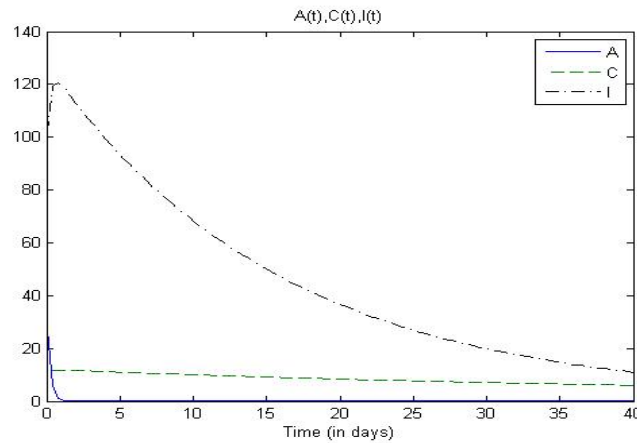


FIGURE 4. With parameters values  $\beta = 0.48, m = 0.02, d_2 = 0.5, \gamma = 0.02, d_3 = 0.01$ .

#### 4. Conclusion

In this work, we introduced a hepatitis B virus stochastic transition model with vaccination and awareness campaign. First, we investigated the asymptotic behavior of vaccination and awareness campaign, through the unique positive solution of our stochastic model. Then we studied different scenarios in order to identify the best control. Graphical justification is also presented.

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