Research Article

Stability Analysis of Hepatitis B Virus Model with Incomplete Immunization of HepB Vaccine

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1. Introduction

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV) and is a major global health problem. According to the data of World Health Organization (WHO), more than 2,000 million people have been infected with HBV and about 350 million remain infected chronically. Every year there are over 4 million acute clinical cases of HBV and about 25% of carriers. Hepatitis B causes about 1 million people to die from chronic active hepatitis, cirrhosis, or primary liver cancer annually [1].

The transmission of HBV occurs normally on contact with infected blood or body fluids. In high prevalence populations, transmission is largely vertical, that is, through mother to child during delivery or horizontal through household contact as skin breaches, open sores, or scratches in the early years of life. In contrast, HBV transmission in low endemicity populations typically occurs in adults via parenteral exposures and intravenous drug use or through sexual contact [2]. It can cause acute and chronic infection status. In acute infection status the individuals have highly infectiousness, and about 90% of adults who are infected with HBV will recover and be completely rid of the virus within six months. The rest of acute infectors turn into chronic infectors and acute hepatitis B occurs rarely in infants. The major routes of chronic hepatitis B infection are mother-infant vertical transmission and early childhood horizontal transmission [3]. Only a small fraction of chronic infectors could be cured completely [4]. Continuous chronic HBV infection exhibits various kinds of clinical symptoms, such as hepatocirrhosis and even hepatocellular carcinoma [5].

Vaccination is an effective control measures for HBV infection, an universal vaccination programme promoted in more than 170 countries since 1982 [6]. In New Zealand, the widespread introduction of infant hepatitis B vaccination in 1988 led to a dramatic decline in cases of acute HBV infection [7]. From 2002, the Ministry of Health of China integrated the infant HepB vaccination into the national immunization program with vaccine provided entirely by the government. According to 2006–2010 hepatitis B control program, China will consistently strengthen the general newborn hepatitis B vaccination and especially supply the first dose of 3-dose HepB series as soon as possible after birth [8].

Mathematical models have been used frequently to study the transmission dynamics of HBV, and qualitative results on such models can be found. Anderson and May first used a simple mathematical model to illustrate the effects of carriers on the transmission of HBV [9]. Thornley et al.
[10] develop a hepatitis B mathematical model, proposed by
Medley et al. [11], that was used to develop a strategy for
eliminating the HBV spread in New Zealand in 2008. Zou
et al. also proposed a mathematical model to understand the
transmission dynamics and prevalence of HBV in mainland
China [12]. Pang et al. [13] develop a model to explore the
impact of vaccination and other controlling measures of
HBV infection and a mathematical model which describes
the spread of HBV is formulated in [14]. Zou et al. [15]
propose an age structure model to predict the dynamics of
HBV transmission and evaluate the long-term effectiveness
of the vaccination programme in China. Wang et al. proposed
and analyzed the hepatitis B virus infection in a diffusion
model confined to a finite domain [16]. A hepatitis B virus
(HBV) model with spatial diffusion and saturation response
of the infection rate is investigated by Xu and Ma [17].
Transmission model of hepatitis B virus with the migration
effect is presented by Khan et al. [18] who analyzed the effect
of immigrants in the model to study the effect of immigrants
for the host population.

In the above literatures, most models involving HepB
vaccine strategy often assumed that the vaccine is completely
effective in preventing the infection of vaccinated individuals.
In fact, it is well known to all that the HepB vaccine should
be taken in three doses at 0, 1, and 6 months. Usually 30–
50% of individuals will gain anti-HBs antibody after the first
dose, 80–90% will gain after the second dose, and almost all
the individuals will have high anti-HBs concentrations one
month after the last dose that 99.8% of vaccinees gained anti-
HBs antibody [19]. So, as soon as the susceptible individuals
begin the vaccination process, they are different from sus-
ceptible individuals. But they should also be distinguished
from recovered individuals who have immunity against the
disease. It means that a few of vaccinated individuals may still
be susceptible to infection, but they will be infected at a lower
rate than unvaccinated susceptible individuals. Epidemic
models including incomplete immune compartment have
been studied in [20–24], but the HBV transmission with the
incomplete HepB vaccine immune is rarely considered.

Motivated by the above consideration, and based on
the natural course of HBV infection, we promote a novel
model to describe the transition dynamic of HBV. It is more
reasonable to consider the impulsive vaccination strategy
for the susceptible individuals; there are fewer literatures
that researched HBV infection with impulsive vaccination
already [25, 26]. We also consider the incomplete immune
compartment in our model.

The remaining parts of this paper are organized as follows.
In Section 2, we formulate the model. In Section 3, we study
the global asymptotic stability of disease-free periodic solu-
tion and the conditions for the permanence of the disease by
comparison techniques. Numerical simulations are presented
in Section 4. In Section 5, we conclude this paper with some
remarks.

2. Modeling

Based on the fact that HepB vaccination is not completely
effective, we improve the model of Zou et al. [12] in three
aspects. Firstly, we considered that vaccinated individuals
may still be susceptible to infection. Secondly, we studied
impulsive vaccination strategy for the susceptible individuals.
Finally, we add a latent period \( \tau \). We divide the population
into six epidemiological groups: the susceptible individuals
to infection \( S \); latently infected \( L \); those acute infectors
\( I_1 \); chronic sufferers \( I_2 \); and recovered \( R \); \( V \) denotes
the density of vaccinees who have begun the vaccination process.
The individuals in \( V \) are different from those in \( S \) and \( R \);
The immune system will create antibody of HBV because
vaccination doses are taken during this process, but it may not
be in a fully protective level. According to the characteristics
of HBV transmission, the flow diagram is shown in Figure 1.
The mathematical model of the transmission dynamics
and prevalence of HBV is as follows:

\[
\begin{align*}
S'(t) &= \mu_0 (1 - v_2) + \varphi V - (\mu + \beta_1 + \varepsilon \beta_2) S, \\
L'(t) &= (\beta_1 I_1 (t - \tau) + \varepsilon \beta_2 (t - \tau)) \\
&\times \left( S(t - \tau) + \vartheta V(t - \tau) \right) - \mu L, \\
I_1'(t) &= e^{-\mu T} (\beta_1 I_1 (t - \tau) + \varepsilon \beta_2 (t - \tau)) \\
&\times \left( S(t - \tau) + \vartheta V(t - \tau) \right) - (\mu + \gamma_1) I_1, \\
I_2'(t) &= \mu_0 v_2 I_2 + q_2 \gamma_1 I_1 - (\mu + \mu_1 + \gamma_2) I_2, \\
V'(t) &= \mu (1 - \omega) - \theta (\beta_1 I_1 + \varepsilon \beta_2) V - (\mu + \varphi) V, \\
R'(t) &= (1 - q) \gamma_1 I_1 + \gamma_2 I_2 - \mu R, \\
&\quad t \neq nT, \quad n \in \mathbb{Z}^+ \\
S(t^+) &= (1 - p) S(t), \\
V(t^+) &= V(t) + pS(t), \\
&\quad t = nT, \quad n \in \mathbb{Z}^+. 
\end{align*}
\]

In these equations, all the parameters are nonnegative, \( \mu \) is the
per capita natural death rate and the birth rate of newborns,
and \( \mu_1 \) is the per capita disease-induced death rate. \( \beta \) is the
transmission coefficient of acute HBV, and \( \varepsilon \beta \) is the reduced
transmission coefficient of chronic HBV. \( \omega \) is the proportion
of births without successful vaccination. \( \gamma_1 \) is the rate at which
individuals leave the acute infection class; a proportion \( 1 - q \)
of acute infectors become chronic carriers and other proportion \( q \)
of acute infection individuals become chronic carriers and other
proportion \( 1 - q \) remain as acute infectors. \( v \) is the proportion of
unimmunized children born to chronic
carrier mothers who have been infected (ignore perinatal
infection of children born to mothers with acute infection).
That \( \mu_0 v_2 I_2 \) denotes newborns who have been infected
in perinatal infection and in chronic infection compartment,
the rest \( \mu_0 (1 - v_2) \) newborns become susceptible individuals.
Figure 1: Flow diagram of HBV transmission in a population.

The factor $\theta$ ($0 < \theta < 1$) reflects the efficacy of vaccine, which means that the vaccine is not completely effective and that the vaccinated individuals have only partial immunity. For the vaccinated individuals, let $\varphi$ denote the per capita rate coefficient at which the immunity wears off, which implies that the vaccinated individuals have the temporary immunity. $p$ ($0 < p < 1$) is the fraction of impulsive vaccination, and $\tau$ is latent period. The period of vaccination is $T$, and the vaccination is dose at time $t = nT$, $n \in N = \{1, 2, 3, \ldots \}$.

Since the equations for the variables $L$ and $R$ in model (1) are both independent of other equations, then the dynamical behavior of (1) is determined by the following system:

\[
\begin{align*}
S'(t) &= \mu \omega (1 - \nu I_2) + \varphi V - (\mu + \beta_1 I_1 + \epsilon \beta_2 I_2) S, \\
I_1'(t) &= e^{-\mu T} (\beta_1 (t - \tau) + \epsilon \beta_2 (t - \tau)) \\
& \quad \times (S(t - \tau) + \theta V(t - \tau)) - (\mu + \gamma_1) I_1, \\
I_2'(t) &= \mu \omega I_2 + q \gamma_1 I_1 - (\mu + \mu_1 + \gamma_2) I_2, \\
V'(t) &= \mu (1 - \omega) - \theta (\beta_1 + \epsilon \beta_2) V - (\mu + \varphi) V, \\
\end{align*}
\]

For ($S + I_1 + I_2 + V$) $\leq \mu [1 - (S + I_1 + I_2 + V)]$ it follows that $\sup_{t \to \infty} (S + I_1 + I_2 + V) \leq 1$. Set $\Omega = \{(S + I_1 + I_2 + V) \in R^4_+ : S + I_1 + I_2 + V \leq 1\}$ is positively invariant of system (2).

Subsequently, we introduce the following lemma, which is useful for the later proof.

**Lemma 1.** Consider the following impulsive differential equation:

\[
\begin{align*}
S'(t) &= \mu \omega - \mu S + \varphi V, \\
V'(t) &= \mu (1 - \omega) - (\mu + \varphi) V, \\
S(t^+) &= (1 - p) S(t), \\
V(t^+) &= V(t) + p S(t), \\
& \quad t \neq nT, \quad n \in Z^+. \\
\end{align*}
\]

Then the above system has a unique positive periodic solution given by

\[
\begin{align*}
S(t) &= \frac{\mu \omega + \varphi}{\mu + \varphi} - \left( V^* - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\frac{(\mu + \varphi)(t - nT)}{\mu + \varphi}}, \\
V(t) &= \frac{\mu (1 - \omega)}{\mu + \varphi} + \left( V^* - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\frac{(\mu + \varphi)(t - nT)}{\mu + \varphi}}.
\end{align*}
\]

Consider that $nT < t \leq (n + 1)T$, which is globally asymptotically stable, where

\[
\begin{align*}
S^* &= \frac{(1 - p) (\varphi + \mu \omega) (1 - e^{(\mu + \varphi)T})}{(\mu + \varphi) [1 - (1 - p) e^{-(\mu + \varphi)T}]}, \\
V^* &= \frac{p (\mu + \varphi) + \mu (1 - p) (1 - \omega) [1 - e^{-\mu \varphi T}] }{(\mu + \varphi) [1 - (1 - p) e^{-\mu \varphi T}]}.
\end{align*}
\]
Proof. It is easy to obtain the analytical solution of (4) between pulses as follows:

\[ S(t) = \frac{\phi + \omega \mu}{\mu + \varphi} + \left[ S(nT^+) + V(nT^+) - 1 \right] e^{-\rho (t-nT)} \]

\[ - \left( V(nT^+) - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (t-nT)}, \]

\[ V(t) = \frac{\mu (1 - \omega)}{\mu + \varphi} + \left( V(nT^+) - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (t-nT)}, \]

\[ nT \leq t \leq (n+1)T. \]  

Furthermore, after each successive pulse, we can deduce the following stroboscopic map:

\[ S((n+1)T^+) = (1-p) \left\{ \frac{\phi + \omega \mu}{\mu + \varphi} + \left[ S(nT^+) + V(nT^+) - 1 \right] e^{-\rho (T)} \right\} \]

\[ - (1-p) \left( V(nT^+) - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (T)}, \]

\[ V((n+1)T^+) = \frac{\mu (1 - \omega)}{\mu + \varphi} + \left( V(nT^+) - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) \left( 1 - e^{-\rho (T)} \right) \]

\[ + \left( V(nT^+) - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) \left( 1 - e^{-\rho (T)} \right) + \frac{p (\phi + \omega \mu)}{\mu + \varphi} \left( 1 - e^{-\rho (T)} \right). \]  

Denote \( x_n = S(nT^+), y_n = V(nT^+) \); then we have the following equations:

\[ x_{(n+1)} = (1-p) \left\{ \frac{\phi + \omega \mu}{\mu + \varphi} + \left[ x_n + y_n - 1 \right] e^{-\rho (T)} \right\} \]

\[ - (1-p) \left( y_n - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (T)}, \]

\[ y_{(n+1)} = \frac{\mu (1 - \omega)}{\mu + \varphi} + px_n e^{-\rho (T)} + \frac{p (\phi + \omega \mu)}{\mu + \varphi} \left( 1 - e^{-\rho (T)} \right) \]

\[ + \left( x_n - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) \left( 1 - e^{-\rho (T)} \right) + \frac{p (\phi + \omega \mu)}{\mu + \varphi} \left( 1 - e^{-\rho (T)} \right). \]  

The unique positive fixed point is \((x^*, y^*)\), where

\[ x^* = \frac{(1-p) (\phi + \omega \mu) \left( 1 - e^{-\rho (T)} \right)}{(\mu + \varphi) \left( 1 - (1-p) e^{-\rho (T)} \right)}, \]

\[ y^* = \frac{p (\mu + \varphi) + \mu (1-p) (1-\omega) \left( 1 - e^{-\rho (T)} \right)}{(\mu + \varphi) \left( 1 - (1-p) e^{-\rho (T)} \right)}. \]

So, (4) has a unique period solution with initial values of \( S(0^+) = x^*, V(0^+) = y^* \). \( \square \)

In the following we prove the global stability of the period solution, and it suffices to prove the global stability of the fixed point \((x^*, y^*)\). The proof is similar to the proof of Lemma 2.1 in [22], so we omit the subsequent proof.

**Lemma 2** (see [27]). Assume that the sequence \( \{t_k\} \) satisfies \( 0 \leq t_0 < t_1 < t_2 \cdots \) with \( \lim_{k \to \infty} t_k = \infty \). Let \( f(t, x) : R^+ \to R^n \) be quasi-monotone nondecreasing in \( x \) for each \( t \), and \( \varphi_k(u) \in C[R^+, R^n] \) is nondecreasing in \( u \) for \( k = 1, 2, \ldots \). Suppose that \( u(t), v(t) \in PC([t_0, \infty), R^n) \) satisfy

\[ D^+ u(t) \leq f(t, u(t)), \quad t \geq t_0, \]

\[ u(t_k) \leq \varphi_k(u(t_k)), \quad k \in N, \]

\[ D^+ v(t) \geq f(t, v(t)), \quad t \geq t_0, \]

\[ v(t_k) \geq \varphi_k(v(t_k)), \quad k \in N. \]

Then \( u_0 \leq v_0 \) implies that \( u(t) \leq v(t) \) for \( t \geq t_0 \).

**Lemma 3** (see [28]). Consider the following equation:

\[ u'(t) = a_1 u(t - \tau) - a_2 u(t), \quad \text{where} \quad a_1 > 0, \quad a_2 > 0, \quad \tau > 0, \quad \text{and} \quad u(t) > 0 \]

for \( -\tau \leq t \leq 0 \). We have

\[ \lim_{t \to -\infty} u(t) = \begin{cases} 0, & \text{if} \quad a_1 < a_2, \\ +\infty, & \text{if} \quad a_1 > a_2. \end{cases} \]

### 3. Stability and Persistence

#### 3.1. Global Stability of the Disease-Free Periodic Solution

Now we will prove the disease-free periodic solution \((\bar{S}(t), 0, 0, \bar{V}(t))\) is locally stable and globally attractive. We first demonstrate the existence of the disease-free periodic solution, in which infectious individuals are entirely absent from the population permanently; that is, \( I_1(t) \equiv 0 \) and \( I_2(t) \equiv 0 \) for all \( t > 0 \). Under this condition, the growth of susceptible individuals must satisfy

\[ S'(t) = \mu \omega - \mu S + \varphi V, \]

\[ V'(t) = \mu (1 - \omega) - \left( \mu + \varphi \right) V, \]

\[ t \neq nT, \quad n \in Z^+ \]

\[ S(t^+) = (1 - p) S(t), \]

\[ V(t^+) = V(t) + p S(t), \]

\[ t = nT, \quad n \in Z^+. \]  

By Lemma 1, we obtain the periodic solution of system (13):

\[ \bar{S}(t) = \frac{\mu \omega + \varphi}{\mu + \varphi} + \left( V^* - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (t-nT)}, \]

\[ \bar{V}(t) = \frac{\mu (1 - \omega)}{\mu + \varphi} + \left( V^* - \frac{\mu (1 - \omega)}{\mu + \varphi} \right) e^{-\rho (t-nT)}, \]

\[ nT \leq t \leq (n+1)T. \]
where

\[ S^* = \frac{(1-p)(\varphi + \mu)\omega}{(\mu + \varphi)\omega}(1-e^{-(\mu+\varphi)T}) \],

\[ V^* = \frac{\rho(\mu + \varphi) + \mu(1-p)(1-\omega)(1-e^{-(\mu+\varphi)T})}{(\mu + \varphi)(1-e^{-(\mu+\varphi)T})} \].

is globally asymptotically stable. Hence, the system (2) has a disease-free periodic solution \( \tilde{S}(t), 0, 0, \tilde{V}(t) \).

Denote

\[ R_1 = e^{\mu T} \int_0^T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-q)} dt \],

\[ R_2 = e^{\mu T} \int_0^T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-\omega)} dt \].

**Theorem 4.** Let \( (S(t), I_1(t), I_2(t), V(t)) \) be any solution of (2); then the disease-free periodic solution \( \tilde{S}(t), 0, 0, \tilde{V}(t) \) is globally asymptotically stable provided that \( R_1 < 1 \) and \( R_2 < 1 \).

**Proof.** Since \( R_1 < 1 \) and \( R_2 < 1 \), we can choose \( \epsilon_1 > 0 \) sufficiently small such that

\[ e^{-\mu T} \int_0^T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-q)} dt < T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-q)} \],

\[ e^{-\mu T} \int_0^T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-\omega)} dt < T \frac{\beta(\tilde{S}+\tilde{V})}{\mu + (1-\omega)} \].

From the equations of system (2), we have \( S'(t) = \mu \omega - \mu S + \varphi V 

and \( V'(t) = \mu (1-\omega) - (\mu + \varphi) V \); then we consider the following comparison system with pulse:

\[ s'(t) = \mu \omega - \mu s + \varphi v, \]

\[ v'(t) = \mu (1-\omega) - (\mu + \varphi) v, \]

\[ nT, \quad n \in \mathbb{Z}^+ \]

\[ s(t^+) = (1-p)s(t), \]

\[ v(t^+) = v(t) + ps(t), \]

\[ t = nT, \quad n \in \mathbb{Z}^+ \].

In view of Lemma 1, we obtain

\[ s(t) = \frac{\mu \omega + \varphi}{\mu + \varphi} - \left(v^* - \frac{\mu (1-\omega)}{\mu + \varphi}\right)e^{-(\mu+\varphi)(t-nT)}, \]

\[ v(t) = \frac{\mu (1-\omega)}{\mu + \varphi} + \left(v^* - \frac{\mu (1-\omega)}{\mu + \varphi}\right)e^{-(\mu+\varphi)(t-nT)}, \]

where

\[ s^* = \frac{(1-p)(\varphi + \mu)\omega}{(\mu + \varphi)\omega}(1-e^{-(\mu+\varphi)T}) \],

\[ v^* = \frac{\rho(\mu + \varphi) + \mu(1-p)(1-\omega)(1-e^{-(\mu+\varphi)T})}{(\mu + \varphi)(1-e^{-(\mu+\varphi)T})} \].

By Lemma 2 there exists an integer \( k_1 \), such that

\[ S(t) \leq s(t) + \epsilon_1 = S_\Delta, \]

\[ V(t) \leq v(t) + \epsilon_1 = V_\Delta, \]

\[ nT < t \leq (n+1)T, \quad n > k_1. \]

Furthermore, from the second and third equations, we have

\[ I_1'(t) + I_2'(t) \leq [e^{-\mu T} \beta(S_\Delta + \theta V_\Delta) I_1(t) - (\mu + (1-q) \gamma_1) I_1(t)] + [\epsilon \beta e^{-\mu T} (S_\Delta + \theta V_\Delta) I_2(t) - (\mu - \mu \omega + \mu_1 + \gamma_2) I_2(t)], \]

for \( t \neq nT, \quad n > k_1 \). Then, according to (17) and Lemma 3, we have \( I_1'(t) + I_2'(t) \leq 0 \). So, \( \lim_{t \to +\infty} (I_1(t) + I_2(t)) = 0 \); there must exist an integer \( k_2 > k_1 \), such that \( I_1(t) < \epsilon_2, I_2(t) < \epsilon_3 \) for all \( t > k_2 T \).

When \( t > k_2 T \), from the first equation of system (2), we have

\[ S'(t) > \mu \omega (1-\omega) - (\mu + \varphi) V \]

\[ V'(t) > \mu (1-\omega) - \theta (\beta \epsilon_2 + \epsilon \beta \epsilon_3) V - (\mu + \varphi) V \]

Consider the following comparison impulsive differential equation for all \( t > k_2 T \):

\[ s_1'(t) = \mu \omega (1-\omega) - (\mu + \varphi) s_1, \]

\[ v_1'(t) = \mu (1-\omega) - \theta (\beta \epsilon_2 + \epsilon \beta \epsilon_3) v_1 - (\mu + \varphi) v_1, \]

\[ t \neq nT, \quad n \in \mathbb{Z}^+ \]
By Lemma 1, we have the unique periodic solution of system (25) given by

\[ \bar{s}_1 = \frac{\mu \omega (1 - \nu e_3) + \varphi}{\varphi + \mu + \beta e_2 + \epsilon \beta e_3} \]

\[ \times e^{-[\beta (\epsilon e_2 + \beta e_3) + \mu + \epsilon \beta] (t - nT)}, \]

\[ \bar{v}_1 = \frac{\mu (1 - \omega)}{(\mu + \varphi) \theta (\beta e_2 + \epsilon \beta e_3)} \]

\[ + \left( \frac{\mu (1 - \omega)}{(\mu + \varphi) \theta (\beta e_2 + \epsilon \beta e_3)} \right) \]

\[ \times e^{-[\beta (\epsilon e_2 + \beta e_3) + \mu + \epsilon \beta] (t - nT)}, \]

(26)

where

\[ s_1^* = \frac{(1 - p)(\mu \omega (1 - \nu e_3) + \varphi)}{(\varphi + \mu + \beta e_2 + \epsilon \beta e_3) [1 - (1 - p)e^{-[\beta (\epsilon e_2 + \beta e_3) + \mu + \epsilon \beta] T}]}, \]

\[ v_1^* = \left( p (\varphi + \mu + \beta e_2 + \epsilon \beta e_3) \right) \]

\[ + \frac{\mu (1 - \omega)(1 - p)(1 - \omega)}{[1 - e^{-[\beta (\epsilon e_2 + \beta e_3) + \mu + \epsilon \beta] T}]} \]

\[ \times [1 - (1 - p)e^{-[\beta (\epsilon e_2 + \beta e_3) + \mu + \epsilon \beta] T}]^{-1}. \]

(27)

By comparison theorem, there exists an integer \( k_3 > k_2 \) such that

\[ S(t) > s_1(t) > \bar{s}_1 - \epsilon_4, \]

\[ V(t) > v_1(t) > \bar{v}_1 - \epsilon_4, \]

\[ nT < t \leq (n + 1) T. \]

(28)

Because \( \epsilon_1, \epsilon_2, \epsilon_3, \) and \( \epsilon_4 \) are sufficiently small, it follows from (22) and (28) that \( \lim_{t \to \infty} S(t) = S^*(t), \lim_{t \to \infty} V(t) = V^*(t). \) Therefore, the disease-free solution \( (S(t), 0, 0, V(t)) \) of system (2) is globally attractive. The proof is completed.

Theorem 4 determines the global attractiveness of (2) in \( \Omega \) for the cases \( R_1 < 1 \) and \( R_3 < 1. \) Its epidemiological implication is that the infectious population vanishes in time so the disease dies out.

3.2. Persistence. In this section we say the disease is endemic if the infectious population persists above a certain positive level for sufficiently large time. The endemicity of the disease can be well captured and studied through the notion of uniform persistence.

Definition 5. System (2) is said to be uniformly persistent if there exist positive constants \( M_i \geq m_i, i = 1, 2, 3 \) (both are independent of the initial values), such that every solution \( (S(t), I_1(t), I_2(t), V(t)) \) with positive initial conditions of system (2) satisfies

\[ m_1 \leq S(t) \leq M_1, \]

\[ m_2 \leq I_1(t) + I_2(t) \leq M_2, \]

\[ m_3 \leq V(t) \leq M_3. \]

Theorem 6. If \( R_1 > 1 \) and \( R_3 > 1, \) then there is a positive constant \( m_1 \) such that each positive solution \( (I_1(t), I_2(t)) \) of system (2) satisfies \( I_1(t) + I_2(t) \geq m_1 \) for all \( t \) sufficiently large.

Proof. Let \( (S(t), I_1(t), I_2(t), V(t)) \) be any solution with initial values of system (2); then it is obvious that \( S(t) \leq 1, I_1(t) \leq 1, I_2(t) \leq 1, \) and \( V(t) \leq 1 \) for all \( t > 0. \) We are left to prove that there exist positive constants \( m_1, m_1, m_2, \) and \( t_0 \) \( (t_0 \) is sufficiently large) such that \( S(t) \geq m_1, I_1(t) + I_2(t) \geq m_1, \) and \( V(t) \geq m_2 \) for all \( t > t_0. \)

Firstly, from the first equation of system (2), we have

\[ S'(t) > \mu \omega (1 - \nu) - (\mu + \beta + \epsilon \beta) S + \varphi V, \]

\[ V'(t) > \mu (1 - \omega) - (\mu + \varphi + \theta (\beta + \epsilon \beta)) V. \]

(30)

Consider the following comparison equations:

\[ u_1'(t) = \mu \omega (1 - \nu) - (\mu + \beta + \epsilon \beta) S + \varphi V, \]

\[ u_2'(t) = \mu (1 - \omega) - (\mu + \varphi + \theta (\beta + \epsilon \beta)) V, \]

\[ t \neq nT, \quad n \in Z^+. \]

(31)

By Lemma 1 and the comparison theorem there exist \( u_1^*, u_2^*; \) we know that for any sufficiently small \( \epsilon_0 > 0, \) there exists a \( t_0 \) \( (t_0 \) is sufficiently large) such that

\[ S(t) \geq u_1(t) - \epsilon_0 = m_1 > 0, \]

\[ V(t) \geq u_2(t) - \epsilon_0 = m_2 > 0. \]

(32)

Next, we will prove that there exist \( m_1 > 0 \) and a sufficiently large \( t_0 \) such that \( I_1(t) + I_2(t) \geq m_1 \) for all \( t > t_0. \)

Since \( R_1 > 1 \) and \( R_3 > 1, \) there exist \( m_i^* > 0 \) and \( \bar{I} > 0 \) sufficiently small such that

\[ e^{-\rho t} \int_0^T [\beta (\eta_1 + \theta \eta_2)] - T(\mu + (1 - q) \gamma_1) > 0, \]

\[ e^{-\rho t} \int_0^T [\epsilon \beta (\eta_1 + \theta \eta_2)] + T[\mu \omega - (\mu + \mu_1 + \gamma_2)] > 0, \]

(33)

where \( \eta_1 \) and \( \eta_2 \) are as in (38).

We claim that for any \( t_0 > 0, \) it is impossible that \( I_1(t) + I_2(t) < m_i^* \) for all \( t \geq t_0. \) Suppose that the claim is not valid.
There exists a $t_0 > 0$ such that $I_1(t) + I_2(t) < m_1^*$ for all $t \geq t_0$. It follows from the first and fourth equations of system (2) that for $t \geq t_0$,
\begin{align*}
S'(t) &> \mu \omega (1 - um_1^*) - (\mu + \beta m_1^* + \epsilon \beta m_1^*) S + \varphi V, \\
V'(t) &> \mu (1 - \omega) - [\mu + \varphi + \theta (\beta m_1^* + \epsilon \beta m_1^*)] V.
\end{align*}
(34)

Consider the comparison impulsive system for $t \geq t_0$:
\begin{align*}
u_3'(t) &= \mu \omega (1 - um_1^*) - (\mu + \beta m_1^* + \epsilon \beta m_1^*) S + \varphi V, \\
u_4'(t) &= \mu (1 - \omega) - (\mu + \varphi + \theta (\beta m_1^* + \epsilon \beta m_1^*)) V,
\end{align*}
\begin{align*}
t &\neq nT', \quad n \in \mathbb{Z}^+.
\end{align*}
(35)

According to Lemma 1, (35) have unique periodic solution
\begin{align*}
\tilde{u}_3 &= \frac{\mu \omega (1 - um_1^*) + \varphi}{\varphi + \mu + \beta m_1^* + \epsilon \beta m_1^*} \\
&\quad - \left( \frac{\mu (1 - \omega)}{\varphi + \mu + \beta m_1^* + \epsilon \beta m_1^*} \right) e^{-[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] (t - nT')}, \\
\tilde{u}_4 &= \frac{\mu (1 - \omega)}{(\varphi + \mu + \beta m_1^* + \epsilon \beta m_1^*)} \\
&\quad + \left( \frac{\mu (1 - \omega)}{\varphi + \mu + \beta m_1^* + \epsilon \beta m_1^*} \right) e^{-[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] (t - nT')},
\end{align*}
(36)

where
\begin{align*}
u_3^* &= \left( (1 - p) \left( \mu \omega (1 - um_1^*) + \varphi \right) \right) \\
&\quad \times \left( 1 - e^{[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] T} \right), \\
&\quad \times \left( \varphi + \mu + \beta m_1^* + \epsilon \beta m_1^* \right) \\
&\quad \times \left( \left[ 1 - (1 - p) e^{-[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] T} \right]^{-1} \right), \\
u_4^* &= \left( p \left( \varphi + \mu + \beta m_1^* + \epsilon \beta m_1^* \right) \right) \\
&\quad + \left( (1 - p) (1 - \omega) \left[ 1 - e^{-[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] T} \right] \right) \\
&\quad \times \left( \varphi + \mu + \beta m_1^* + \epsilon \beta m_1^* \right) \\
&\quad \times \left( \left[ 1 - (1 - p) e^{-[\theta (\beta m_1^* + \epsilon \beta m_1^*) + \mu + \varphi] T} \right]^{-1} \right).
\end{align*}
(37)

So there exists $T_1 > t_0$ such that
\begin{align*}
S(t) &> \tilde{u}_3(t) - \varepsilon = \eta_1, \\
V(t) &> \tilde{u}_4(t) - \varepsilon = \eta_2,
\end{align*}
(38)

for all $t > T_1$.

We denote
\begin{align*}
\Pi(t) &= I_1(t) + I_2(t) \\
&\quad + \beta e^{-\rho T} \int_{t-T}^{t} I_1(\xi) [S(\xi) + \theta V(\xi)] d\xi, \\
&\quad + \beta e^{-\tau T} \int_{t-T}^{t} I_2(\xi) [S(\xi) + \theta V(\xi)] d\xi.
\end{align*}
(39)

From (2), we have
\begin{align*}
\Pi'(t) &= \left[ \beta e^{-\rho T} (S + \theta V) - (\mu + (1 - q) \gamma_1) \right] I_1(t) \\
&\quad + \left[ \beta e^{-\tau T} (S + \theta V) - (\mu + (1 - q) \gamma_2) \right] I_2(t) \\
&\quad \geq \left[ \beta e^{-\tau T} (\eta_1 + \theta \eta_2) - (\mu + (1 - q) \gamma_1) \right] I_1(t) \\
&\quad + \left[ \beta e^{-\rho T} (\eta_1 + \theta \eta_2) - (\mu + (1 - q) \gamma_2) \right] I_2(t)
\end{align*}
(40)

for $t > T_1$.

From (33), we obtain $\Pi'(t) > 0$, for $t > T_1$, which implies that $\Pi(t) \to \infty$, $t \to \infty$. This is contrary to the fact that $\Pi(t)$ is bounded. Hence, there exists a $t_1 > 0$ such that $I_1(t_1) + I_2(t_1) \geq m_1^*$.

Next we prove that there exists a $m_1^*$ such that any positive solution of (2) satisfies $\lim_{t \to \infty} \inf t_{i+1} I_1(t) + I_2(t) > m_1^*$.

Define
\begin{align*}
m_1^* &= \min \left\{ \frac{m_1^*}{2}, q_1 \right\}, \\
q_1 &= m_1^* e^{-\Lambda T},
\end{align*}
(41)

where $\Lambda = \max\{\mu + (1 - q) \gamma_2, (1 - \omega) \mu + \mu_1 + \gamma_2\}$.

First, if $I_1(t) + I_2(t) > m_1^*$ for all $t > t_1$, then our aim is obtained.

Second $I_1(t) + I_2(t)$ oscillates about $m_1^*$ for all large $t$; setting $t^* = \inf_{t \geq t_1} I_1(t) + I_2(t) \leq m_1^*$, there are two possible cases for $t^*$.

We hope to show that $I_1(t) + I_2(t) \geq m_1^*$ for all large $t$. The conclusion is evident in the first case. For the second case, let $t^* > 0$ and $p > 0$ satisfy $I_1(t^*) + I_2(t^*) = I_1(t^* + \rho) + I_2(t^* + \rho) = m_1^*$, and $I_1(t) + I_2(t) < m_1^*$, $S(t) > \eta$ for $t^* < t < t^* + \rho$.

Therefore, it is certain that there exists a $g$ ($0 < g < \tau$) such that
\begin{align*}
I_1(t) + I_2(t) \geq m_1^* / 2 \\
\text{for } t^* < t < t^* + g.
\end{align*}
(42)

In this case, we will discuss three possible cases in terms of the sizes of $g$, $\rho$, and $\tau$.

Case I. If $\rho \leq g \leq \tau$, then $I_1(t) + I_2(t) \geq m_1^* / 2$ for $t^* < t < t^* + \rho$.

Case II. If $g \leq \rho \leq \tau$, then from equations of system (2), we can deduce $I_1'(t) + I_2'(t) > -\Lambda I(t)$, where $\Lambda = \max\{\mu + (1 - q) \gamma_1, (1 - \omega) \mu + \mu_1 + \gamma_2\}$.
The number of susceptible individuals
(a)

The number of latently infected
(b)

The number of acute infectors
(c)

The number of chronic sufferers
(d)

Figure 2: The effect of vaccine efficacy on the number of (a) susceptible individuals, (b) latently infected, (c) acute infectors, and (d) chronic sufferers. The parameters are \( \mu = 0.1; \nu = 0.1; \varphi = 0.1; \beta = 3; \varepsilon = 0.016; \gamma_2 = 0.025; \mu_1 = 0.28; \tau = 10; \omega = 0.2; q = 0.4; \gamma_1 = 0.4; \theta = 0.3; p = 0.6 \); the initial values are \( S(0) = 0.1; L(0) = 0.05; I_1(0) = 0.05; I_2(0) = 0.05; V(0) = 0.1; R(0) = 0.1 \).

\[
\delta_1, (1 - \omega)\mu + \mu_1 + \gamma_2 \quad \text{for} \quad t \in [t^*, t^* + \tau] \quad \text{and} \quad I_1(t^*) + I_2(t^*) = m_i^* \quad \text{it is obvious that} \quad I_1(t) + I_2(t) \geq q_1 \quad \text{for} \quad t^* < t < t^* + \rho.
\]

Case III. If \( g \leq T \leq \rho \), we will consider the following two cases, respectively.

Case IIIa. For \( t^* < t < t^* + \tau \), it is easy to obtain \( I_1(t) + I_2(t) > q_1 \).

Case IIIb. For \( t^* + \tau < t < t^* + \rho \), it is easy to obtain \( I_1(t) + I_2(t) > q_1 \). Then, proceeding exactly as the proof for the above claim, we see that \( I_1(t) + I_2(t) \geq m_i \) for \( t^* + \tau < t < t^* + \rho \). Since this kind of interval \([t^*, t^* + \rho]\) is chosen in an arbitrary way (we only need \( t^* \) to be large), we conclude that \( I_1(t) + I_2(t) \geq m_i \) for all large \( t \) in the second case. In view of our above discussions, the choices of \( m_i \) are independent of the positive solution, and we have proved that any positive solution of (2) satisfies \( I_1(t) + I_2(t) \geq m_i \) for all large \( t \). The proof is completed.

4. Numerical Simulations

In this section, we present some numerical simulations to demonstrate the transmission dynamic of HBV. According to the natural history of HBV transmission and prior research [10, 12], we set some parameter values of the model: \( \mu = 0.1; \nu = 0.1; \varphi = 0.1; \beta = 3; \varepsilon = 0.016; \gamma_2 = 0.025; \mu_1 = 0.28; \tau = 10; \omega = 0.2; q = 0.4; \gamma_1 = 0.4; \theta = 0.3; p = 0.6 \).

And we choose \( \theta = 0.1, 0.3 \), respectively; then number of susceptible individuals, latently infected, acute infectors and chronic sufferers are seen in Figure 2. It is easy to see that the lower of \( \theta \) (the higher of vaccine efficacy) the fewer of the number of infected individuals. So, knowing the efficacy of HBV vaccine is necessary for the extinct of disease.

In order to find better control strategies for HBV infection, we would like to see what parameters can affect the change of the acute infectors number. From Figure 3(a) we can see that the increase of \( p \) and decrease of \( \theta \) will make the number of acute infectors lower. If \( \theta \) is higher, that is to say,
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Figure 3: The graphs of the number of acute infectors with some parameters: (a) $\mu = 0.1; v = 0.1; \varphi = 0.1; \beta = 12; \epsilon = 0.16; \gamma_2 = 0.025; \mu_1 = 0.028; \tau = 5; \gamma_1 = 0.4; q = 0.4; \omega = 0.2; \text{surf } p \in [0, 1], \theta \in [0, 0.3]$. (b) $\mu = 0.1; v = 0.1; \varphi = 0.1; \beta = 12; \epsilon = 0.16; \gamma_2 = 0.025; \mu_1 = 0.028; \tau = 5; \omega = 0.2; q = 0.4; \text{surf } \theta \in [0, 0.3], \gamma_1 \in [0, 0.4]$. (c) $\mu = 0.1; v = 0.1; \varphi = 0.1; \beta = 12; \epsilon = 0.16; \gamma_2 = 0.025; \mu_1 = 0.028; \tau = 5; \omega = 0.2; \gamma_1 = 0.4; q = 0.4; \text{surf } \theta \in [0, 0.3], \omega \in [0, 0.2]$. (d) $\mu = 0.1; v = 0.1; \varphi = 0.1; \beta = 12; \epsilon = 0.16; \gamma_2 = 0.025; \mu_1 = 0.028; \tau = 5; \gamma_1 = 0.4; q = 0.4; \text{surf } \theta \in [0, 0.3], \omega \in [0, 0.2]$.  

the efficacy of vaccination is lower, higher vaccination cannot keep the disease extinct. So, to control the disease spread, knowing the vaccine efficacy is important.

In Figure 3(b) we plot the number of acute infectors which change with parameters $\theta$ and $\gamma_1$. We can see that with the increase of $\gamma_1$ the number of acute infectors decreases even if the efficacy of vaccination is lower. That is to say, take measures to cure the acute infectors in time is a necessary method to decrease the number of acute infectors. So, doing check regularly and treatment at early time are necessary. In Figure 3(c) we find not only the increase of $\gamma_1$ but also the parameter $q$ has effect on the number of acute infections; the higher the acute individuals treatment rate, the lower the number of acute infections.

In Figure 3(d), we detect that the decrease of $\theta$ and $\omega$ will make the number of infected individuals lower. So successful immunization of both newborns and susceptible individuals is an efficient intervention strategy. The optimal control strategy will be a combination of improving the vaccine efficacy, increasing the immunization of newborns and susceptible individuals, and increasing the treatment to the acute infected individuals.

5. Conclusion

Hepatitis B virus is highly prevalent in many countries of the world; we promote a new epidemic model based on the spread characters of the HBV, and consider the fact that the HepB vaccine is incomplete immunization in the vaccination process. Our model is more approach to the realistic problem and different from [13, 14]. Moreover, the methods in disposing the model are different from the existing results because more factors are considered. We find when $R_1 < 1$ and $R_2 < 1$, the disease-free periodic solution is globally attractive; if $R_1 > 1$ and $R_2 > 1$, the disease is permanent by using the comparison theorem of impulsive differential equation. By some simulation experiments, Figures 2 and 3 show some effects of parameters on the number of acute individuals and provides an optimal control strategy for the HBV transmission.
Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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