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The Complex Dynamics of Hepatitis B Infected Individuals with Optimal Control*

DIN Anwarud · LI Yongjin · SHAH Murad Ali

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Abstract This paper proposes various stages of the hepatitis B virus (HBV) besides its transmissibility and nonlinear incidence rate to develop an epidemic model. The authors plan the model, and then prove some basic results for the well-posedness in term of boundedness and positivity. Moreover, the authors find the threshold parameter R_0, called the basic/effective reproductive number and carry out local sensitive analysis. Furthermore, the authors examine stability and hence condition for stability in terms of R_0. By using sensitivity analysis, the authors formulate a control problem in order to eradicate HBV from the population and proved that the control problem actually exists. The complete characterization of the optimum system was achieved by using the 4^{th}-order Runge-Kutta procedure.

Keywords Hepatitis B epidemic model, non-linear incidence, normalized sensitivity index, numerical simulation, optimization theory, reproduction number, stability analysis.

1 Introduction

The study of modeling is one of the influence instrument to understand the time dynamics of various infectious diseases. Numerous of biologists and mathematicians have analyzed mathematical models for the spreading of communicable infections in community[1–12]. HBV infection is one of the severe health problem which caused million of people suffered. Approximately 0.78 million individuals dies each year from the consequences of HBV[13].

It can be transferred by different ways, which include syringes sharing, transfusion of blood and sexual interactions, etc[1, 6]. HBV infection also transfers maternally, i.e., from infected mother to baby, which is known the vertical type of transmission. Utmost infected individual in the acute stage, the immune system have the capability to clear the HBV, however for some

DIN Anwarud · LI Yongjin (Corresponding author)
Department of Mathematics, Sun Yat-sen University, Guangzhou 510275*, China.*
Email: anwarud@mail.sysu.edu.cn; stslyj@mail.sysu.edu.cn.
SHAH Murad Ali
School of Mathematical Sciences; Beijing Normal University, Beijing 100875*, China.*
Email: muradmath@yahoo.com.
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one, especially children are particularly vulnerable and cultivate acute contaminations, which further leads to the chronic carrier and may develop liver cancer. While there are a vaccine and new methods to avoid the transmission. This disease has multiple stages, i.e., acute and chronic. The first one is the primary 6 months period, if some one is exposed. Chronic stage refers to the most serious stage of HBV infection in which serious problems may occur. This infection usually has no history regarding acute stage, but produce scarring of liver and as a result develop failure of liver[14].

Different mathematician and biologists formulated epidemic models to forecast the dynamics of HBV[14–16]. The incidence rate has a vital and major role in studying the modeling of infectious diseases. In sexually transmittable diseases, e.g., HBV, HIV, etc., non-linear incidence is more realistic then other incidence rates. One of the type of incidence rate is bilinear incidence βSI, which was also frequently used[17–19], where β, S and I characterize the interaction rate, the susceptible class, the infectious class respectively. Non-linear incidence rate, which is defined by $\frac{\beta SI}{N}$ used by many authors, see for detail[20, 21]. In this rate, β demonstrates the disease transfer rate, while S, I and N respectively show susceptible population, infected population and total population.

We investigate a model to study the dynamics of HBV transmission and formulate an control mechanism. The current study is actually divided into two main parts, the dynamic and control. In the dynamic part, we discuss and prove the stabilities of the proposed model, however in control part, we plan a control strategy to minimize the infection. More preciously, first, we prove the mathematical properties (boundedness, positivity) to show the well posed-ness and biological feasibility. The threshold quantity will be obtained to discuss the sensitivity analysis. We discuss stability at both equilibrium using the linearization, the Lyapunov theory and geometrical approach. We also investigate a hepatitis B virus elimination mechanism using three control variables (isolation, vaccination and treatment). The control strategy was formulated by using sensitivity of R_0 with respect to (w.r.t) parameters. Moreover, we obtain the optimality condition and discuss the existence of solution. Numerical results will be presented for supporting analytical findings. Finally, we conclude our work.

The organization of the paper is structured as follows: The proposed HBV model is given in Section 2. We deliberate the properties of existence, positive solution, boundedness and biologically feasibility in Section 3. The reproductive number and the equilibria are presented in Section 4. The stability and numerics of the stability results are given in Sections 5 and 6, respectively. In Section 7, we discussed the local sensitivity analysis. The formulation of the optimal control mechanism and its existence of positive solution with optimality condition are respectively presented in Subsections 8.1 and 8.2. Simulations are presented for the verification of the optimization in Section 9. Section 10 is devoted to concluding remarks.

2 Model Formulation

We present the model for HBV spreading with non-linear incidence. According to characteristic of the HBV imposing assumption given by:

a_1. The entire population is shown by by $N(t)$ and is subdivided into 6 different subgroups of $S(t)$ (susceptible/vulnerable), $L(t)$ (exposed/latent), $A(t)$ (acute infected), $C(t)$ (chronic carrier infectious), $R(t)$ (recovered) and $V(t)$ (vaccinated), i.e., $S + A + L + C + V + R = N$, which oi changing w.r.t time t.

a_2. The entry of new born, which are parentally infected will go to carrier class.

a_3. The new born, which are not parentally infected will go to the susceptible class.

a_4. Successful vaccinated individuals go to the vaccinated class.

a_5. Removed population have immunity.

a_6. The new born with effective vaccination will go to vaccination class.

Thus, the above assumptions $a_1 - a_6$ lead to the following model:

$$\begin{aligned}
\frac{dS(t)}{dt} &= \xi b(1-\eta C(t))N + \phi V(t) - \frac{\beta S(t)A(t)}{N} - \frac{\beta}{N}\gamma S(t)C(t) \\
&\quad - (\gamma_3 + d_0)S(t), \quad S(0) > 0, \\
\frac{dL(t)}{dt} &= \frac{\beta A(t)S(t)}{N} + \frac{\gamma\beta C(t)S(t)}{N} - (\sigma + d_0)L(t), \quad L(0) \geq 0, \\
\frac{dA(t)}{dt} &= -(d_0 + \gamma_1)A(t) + \sigma L(t), \quad A(0) \geq 0, \\
\frac{dC(t)}{dt} &= \xi b\eta C(t)N - (d_1 + d_0 + \gamma_2)C(t) + p\gamma_1 A(t), \quad C(0) \geq 0, \\
\frac{dR(t)}{dt} &= \gamma_1(1-p)A(t) + \gamma_2 C(t) - d_0 R(t), R(0) \geq 0, \\
\frac{dV(t)}{dt} &= (1-\xi)bN - (\phi + d_0)V(t) + \gamma_3 S(t), \quad V(0) > 0.
\end{aligned} \tag{1}$$

Table 1 Parameters description of the proposed model (1)

Notation	Parameter description
b	birth rate
ξ	fraction of new-born without effective immunization
η	rate of vertically infected individual
ϕ	induced immunity rate with wane vaccination
β	disease spread rate
γ	reduced transmission rate
d_1, d_0	disease induced and natural death rates
σ	the rate at which people coming to acute class from the latent population
γ_1	rate of acute to chronic
γ_2	the rate at which people coming to recovered class from the carriers population
γ_3	vaccination rate
p	the rate at which recover people fails in acute class

3 Fundamental Properties of the Model

Regarding the fundamental properties of the proposed model (1), we shall prove the following results.

Proposition 3.1 *The orthant R_+^6 is positively invariant for the proposed model presented in* (1).

Proof Assume that $X = (S, L, A, C, R, V)^{\mathrm{T}}$, then the model (1) can be written as

$$\frac{dX(t)}{dt} = GX + H, \tag{2}$$

where

$$G = \begin{pmatrix} -\frac{\beta A(t)}{N} - \frac{\gamma\beta C(t)}{N} - d_0 - \gamma_3 & 0 & -b\xi\eta N & 0 & 0 & \phi \\ \frac{\beta A(t)}{N} + \frac{\gamma\beta C(t)}{N} & -(d_0+\gamma_1) & 0 & 0 & 0 & 0 \\ 0 & \sigma & -(d_0+\gamma_1) & 0 & 0 & 0 \\ 0 & 0 & \gamma_1(1-p) & \gamma_2 & -d_0 & 0 \\ -Y_{11} & 0 & 0 & 0 & 0 & 0 \\ \gamma_3 & 0 & 0 & 0 & 0 & -(d_0+\phi) \end{pmatrix}, \tag{3}$$

$$H = \begin{pmatrix} b\xi N \\ 0 \\ 0 \\ 0 \\ 0 \\ (1-\xi)bN \end{pmatrix}. \tag{4}$$

Clearly matrix $H \geq 0$. Also the off-diagonals of G are nonnegative, which shows that G is Metzler matrix. Thus, the system (1) is positively invariant in R_+^6. ∎

Proposition 3.2 *If $t > 0$ along with non-negative initial condition, the solutions of the model* (1) *are positive, if exist.*

Proof Let $I \subset [0, +\infty)$. If the solution of the system (1) exists in I, then the solution of the 1st equation in the system (1) look like

$$S(t) = \mathrm{e}^{-(\gamma_3+d_0)t - \int_0^t \frac{1}{N}[\beta A(x)+\beta\gamma C(x)]dx}\Bigg[S(0) + \int_0^t \mathrm{e}^{(\gamma_3+d_0)\tau + \int_0^\tau \frac{1}{N}[\beta A(w)+\beta\gamma C(w)]dw} \times \Big(b\xi N(1-\eta C(\tau)) + V(\tau)\phi\Big)d\tau\Bigg]. \tag{5}$$

From Equation (5) it is noted that $S(t) > 0$ only if $A(t)$ and $C(t)$ are positive. From the third equation of the model, we can write

$$A(t) = \mathrm{e}^{-(\gamma_1+d_0)t}A(0) + \mathrm{e}^{-(\gamma_1+d_0)t}\int_0^t \sigma L(\tau)\mathrm{e}^{(\gamma_1+d_0)\tau}d\tau, \tag{6}$$

which shows that $A(t) \geq 0$ whenever $L(t) \geq 0$. Similarly, positivity of $C(t)$ depends on the positivity of A. In the same way, it can be investigated that the other classes $R(t)$ and $V(t)$ are nonnegative, which proves the conclusion. ∎

Remark 3.3 The proposed model (1) is a dynamical system in the following region given by

$$\Omega = \left\{ (S, L, A, C, R, V) \in R_+^6 : N(t) \leq \frac{bN}{d_0} \right\}. \tag{7}$$

4 Threshold Parameter (Basic Reproductive Number) and Equilibria

This section of the manuscript is devoted to finding of the threshold parameter (basic reproductive number) and equilibria of the model.

4.1 Computation of Equilibria and Basic Reproduction Number

The model under consideration (1) has a DFE point denoted by $F_0 = (S_0, 0, 0, 0, 0, V_0)$, where

$$S_0 = \frac{Nb(\phi + \xi d_0)}{d_0(d_0 + \phi + \gamma_3)}, \quad V_0 = \frac{Nb(d_0 - d_0\xi + \gamma_3)}{d_0(d_0 + \phi + \gamma_3)}. \tag{8}$$

In epidemic models, the threshold parameter R_0 has a vital role and is a significant approach. It characterizes the average amount of newly infections. We follow the techniques of Driessche-Watmough[22, 23]. Let $\chi = \big(L, A, C\big)^{\mathrm{T}}$, then by the use of

$$\overline{F} = \begin{pmatrix} \frac{\beta}{N} S(t)A(t) + \frac{\beta\gamma C(t)S(t)}{N} \\ 0 \\ 0 \end{pmatrix}, \quad \overline{W} = \begin{pmatrix} (d_0 + \sigma)L(t) \\ (\gamma_1 + d_0)A(t) - \sigma L(t) \\ (d_1 + d_0 + \gamma_2 - b\xi\eta N)C(t) - p\gamma_1 A(t) \end{pmatrix}, \tag{9}$$

the model (1), yields

$$\frac{d\chi}{dt} = \overline{F} - \overline{W}, \tag{10}$$

where $\overline{W}$ and $\overline{F}$ are the matrices containing the linear and nonlinear terms, respectively. Let $q_2 = d_0 + \sigma$, $q_3 = \gamma_1 + d_0$, $q_4 = -b\xi\eta N + \gamma_2 + d_1 + d_0$ and taking the Jacobian of Equation (9) at DFE point $F_0 = (S_0, 0, 0, 0, 0, V_0)$, which becomes the following

$$F = \begin{pmatrix} 0 & \frac{\beta}{N} S_0 & \frac{\beta\gamma}{N} S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad W = \begin{pmatrix} q_2 & 0 & 0 \\ -\sigma & q_3 & 0 \\ 0 & -p\gamma_1 & q_4 \end{pmatrix}. \tag{11}$$

The dominant eigenvalue ρ, of $\overline{K} = FW^{-1}$ is the threshold quantity, R_0. We find R_0, for the model (1), which has the form, $R_0 = \gamma_{01} + \gamma_{02}$ with

$$\gamma_{01} = \frac{\sigma\beta S_0}{Nq_2q_3}, \quad \gamma_{02} = \frac{\sigma\beta S_0\gamma\gamma_1 p}{Nq_2q_3q_4}, \quad \text{where } S_0 = \frac{bN(d_0 + \phi)}{d_0(d_0 + \phi + \gamma_3)}. \tag{12}$$

Similarly endemic-state of the system (1) is represented by $F_\star = (S_*, L_*, A_*, C_*, R_*, V_*)$ exist, if $R_0 > 1$, where

$$\begin{aligned}
S_* &= \frac{q_2 q_3 q_4}{q_4 + p\gamma\gamma_1}, \quad L_* = \frac{d_0 q_2 q_3^2 q_4(\gamma_3 + q_5)(q_4 - b\xi\eta N)\big(R_0 - 1\big)}{q_5\sigma(p\gamma\gamma_1 + q_4)((q_4 + p\gamma\gamma_1)\beta S_* + b\xi\eta p\gamma_1)}, \\
A_* &= \frac{d_0 q_2 q_3 q_4^2(q_5 + \gamma_3)(R_0 - 1)}{q_5(\gamma_1 p\gamma + q_4)((\gamma_1 p\gamma + q_4)S_*\beta + \xi bN\eta\gamma_1 p)}, \\
C_* &= \frac{\gamma p\beta d_0 q_3\gamma_1(q_5 + \gamma_3)\big(R_0 - 1\big)S_*^2}{q_5((\gamma_1 p\gamma + q_4)\beta S_* + \xi bN\eta\gamma_1 p)}, \quad R_* = \frac{1}{d_0}(1-p)\gamma_1 A_* + \gamma_2 C_*, \\
V_* &= \frac{1}{q_5}((1-\xi)bN + \gamma_3 S_*),
\end{aligned} \tag{13}$$

$q_1 = d_0 + \gamma_3$ and $q_5 = d_0 + \phi$. Clearly, there does not exist a positive endemic-state, if $R_0 < 1$, but the case of $R_0 > 1$, implies the existence of a unique positive equilibrium.

5 Stability Analysis

Usually, epidemic models are used to exhibiting the long-term behavior of an infectious disease. For this purpose, researchers are using the tools of stability analysis as described in [24–27]. To discuss the stability analysis of the proposed model, we prove the following subsequent results.

Remark 5.1 If we assume that $R_0 < 1$, then the DFE of the model is stable locally asymptotically, while unstable, whenever $R_0 > 1$.

Theorem 5.2 *The DFE point F_0 is stable globally asymptotically, if $R_0 < 1$, while unstable, if $R_0 > 1$.*

Proof Assume that $\psi(t) = (S - S_0) + L(t) + A(t) + C(t) + R(t) + (V - V_0)$ and suppose the function defined by

$$\Gamma(t) = \frac{1}{2}\big[\psi(t)\big]^2 + k_1(S - S_0) + k_2 L(t) + k_5(V - V_0) + k_3 A(t) + k_4 C(t), \tag{14}$$

where the positive constants k_i for $i = 1, 2, \cdots, 5$ will be determined later. Differentiating Equation (14) and using the system (1), we get

$$\begin{aligned}
\frac{d\Gamma(t)}{dt} &= \big(\psi(t)\big)(bN - d_0 N(t) - d_1 C(t)) \\
&+k_1\bigg(\phi V(t) + \xi Nb(1 - \eta C(t)) - \frac{\beta A(t)S(t)}{N} - \frac{\beta\gamma C(t)S(t)}{N} - (\gamma_3 + d_0)S(t)\bigg) \\
&+k_2\bigg(\frac{\beta S(t)A(t)}{N} + \frac{\gamma\beta S(t)C(t)}{N} - (\sigma + d_0)L(t)\bigg) + k_3\bigg(-(\gamma_1 + d_0)A(t) + \sigma L(t)\bigg) \\
&+k_4\bigg(\xi b\eta NC(t) + \gamma_1 pA(t) - (d_1 + \gamma_2 + d_0)C(t)\bigg) \\
&+k_5\bigg((1-p)\gamma_1 A(t) + \gamma_2 C(t) - d_0 R(t)\bigg) + k_6\bigg((1-\xi)Nb - (d_0 + \phi)V(t) + \gamma_3 S(t)\bigg).
\end{aligned} \tag{15}$$

By assigning the values of q_2q_4 to K_i where $i = 1, 2, 3, 5$ and $k_4 = \sigma\beta\gamma S_0$, then Equation (15) becomes

$$\begin{aligned}\frac{d\Gamma(t)}{dt} = &-\big(\psi(t)\big)^2 - \big(\psi(t)\big)d_1C(t)\\ &-\xi bN\eta(d_0\sigma)(d_1+\gamma_2+d_0-\xi bN\eta)C(t)\\ &-d_0(d_0+\sigma)(d_0+\gamma_2+d_1-\xi b\eta N)L(t)\\ &-(d_0+\sigma)(d_0+\gamma_1)(d_0+\gamma_2+d_1-\xi bN\eta)(1-\gamma_{02})\\ &-\beta\sigma\gamma(d_0+\gamma_2+d_1-\xi bN\eta)S_0C(t)\\ &-(d_0+\sigma)(d_0+\gamma_2+d_1-\xi bN\eta)((S-S_0)d_0+(V-V_0)).\end{aligned} \tag{16}$$

Equation (16) gives that, if $R_0 < 1$, then $\frac{d\Gamma(t)}{dt} < 0$. Also $\frac{d\Gamma(t)}{dt} = 0$, at the DFE point, therefore, LaSalle's principle assure that F_0 is globally stable. ∎

To perform stability of EE, we shall state and prove the following result.

Theorem 5.3 *The disease EE, $F_* = (S_*, L_*, A_*, C_*, R_*, V_*)$ is stable locally asymptotically whenever $R_0 > 1$, while unstable, if $R_0 < 1$.*

Proof Clearly the recovered compartment only appears in one of the equation of the proposed model. So it is enough to discuss the reduced system without recovered class. Taking the linearize matrix of the system (1) without recovered compartment around F_* and then making use of the elementary row operation we get

$$J(F_*) = \begin{pmatrix} -q_1 - \frac{\beta S_*}{N} - \frac{\gamma\beta S_*}{N} & 0 & -\frac{\beta S_*}{N} & -(b\xi\eta N + \frac{\gamma\beta S_*}{N}) & \phi \\ 0 & -q_2 & H_1 & \gamma H_1 - b\xi\eta H_2 & \phi H_2 \\ 0 & 0 & \frac{H_1}{q_2}\sigma - q_3 & \frac{\sigma}{q_2}(H_1\gamma - \xi b\eta H_2) & \frac{\sigma\phi H_2}{q_2} \\ 0 & 0 & 0 & H_3 - b\xi\eta N H_4 & \phi H_4 \\ 0 & 0 & 0 & 0 & H_5 \end{pmatrix}, \tag{17}$$

where

$$\begin{aligned} H_1 &= \frac{q_1\beta S_*}{A_*\beta + d_0N + \beta\gamma C_* + N\gamma_3}, \quad H_2 = \frac{A_*\beta + \beta^2\gamma C_*}{\beta A_* + d_0N + \beta\gamma C_* + N\gamma_3},\\ H_3 &= -\frac{\beta\gamma p\gamma_1 q_1 S_*}{\beta q_1\sigma S_* - q_3q_2(Nd_0 + A_*\beta + \beta\gamma C_* + N\gamma_3)} - q_4,\\ H_4 &= \frac{\beta\sigma\gamma_1 p(A_* + C_*\gamma)}{q_3q_2(Nd_0 + A_*\beta + \beta\gamma C_* + N\gamma_3) - \beta\sigma q_1 S_*},\\ H_5 &= \frac{\phi\gamma_3 H_4\big(\gamma_1 p(\xi bN^2\eta + \beta\gamma S_*) + \beta S_* q_4\big)}{\gamma_1 p(Nd_0 + A_*\beta + \beta\gamma C_* + N\gamma_3)(H_3 - \eta b\xi H_4 N)}\\ &\quad - \frac{q_5(Nd_1 + A_*\beta + \beta\gamma C_*) + N\gamma_3 d_0}{Nd_0 + A_*\beta + \beta\gamma C_* + N\gamma_3}. \end{aligned} \tag{18}$$

The matrix (17) has the eigenvalues

$$\begin{aligned}
\lambda_1 &= -q_2,\\
\lambda_2 &= -\frac{q_1N+\beta\gamma C_*+\beta A_*}{N},\\
\lambda_3 &= -\frac{q_3q_2(Nd_0+A_*\beta+\beta\gamma C_*+N\gamma_3)-q_1\beta\sigma S_*}{q_2(Nd_0+A_*\beta+\beta\gamma C_*+N\gamma_3)},\\
\lambda_4 &= H_3-\xi bNH_4\eta, \quad \lambda_5 = H_5.
\end{aligned} \tag{19}$$

Clearly, among the above eigenvalues, two eigenvalues λ_1 and λ_2 are negative, while λ_i, for $i=3,4,5$ are negative, if

$$\begin{aligned}
&\frac{\gamma\beta\gamma_1 pS_*}{q_4q_2(Nd_0+A_*\beta+\gamma\beta C_*+N\gamma_3)-\beta\gamma q_4S_*}<1,\\
&\frac{\sigma q_1\beta S_*}{q_2q_3(d_0N+\beta A_*+\beta\gamma C_*+\gamma_3N)}<1,
\end{aligned} \tag{20}$$

which also satisfied. Thus, the eigenvalues of the matrix (17) are negative which proves the conclusion. ∎

Theorem 5.4 *The EE F_* is globally stable, if $R_0>1$, while unstable for $R_0<1$.*

Proof Taking the Jacobian matrix J and the second additive compound matrix $J^{|2|}$ for only the first three equations of the system (1), we get

$$J=\begin{pmatrix} -a_{11} & 0 & -a_{13}\\ a_{21} & a_{22} & a_{23}\\ 0 & \sigma & -a_{33}\end{pmatrix} \text{ and } J^{|2|}=\begin{pmatrix} -(a_{11}+a_{22}) & a_{23} & -a_{13}\\ a_{32} & -a_{11}-a_{33}) & a_{12}\\ -a_{31} & a_{21} & -(a_{22}+a_{33})\end{pmatrix}. \tag{21}$$

Let $P(\chi)=\operatorname{diag}\left\{\frac{S}{L},\frac{S}{L},\frac{S}{L}\right\}=P(S,L,A)$, implies $P^{-1}(\chi)=\operatorname{diag}\left\{\frac{L}{S},\frac{L}{S},\frac{L}{S}\right\}$, then taking the derivative w.r.t, that is, $P_f(\chi)$, we get

$$P_f(\chi)=\operatorname{diag}\left\{\frac{\dot S}{S}-\frac{S\dot L}{L^2},\frac{\dot S}{S}-\frac{S\dot L}{L^2},\frac{\dot S}{S}-\frac{S\dot L}{L^2}\right\}. \tag{22}$$

Now $\operatorname{diag}\left\{\frac{\dot S}{S}-\frac{\dot L}{L},\frac{\dot S}{S}-\frac{\dot L}{L},\frac{\dot S}{S}-\frac{\dot L}{L}\right\}=P_fP^{-1}$ and $J_2^{|2|}=PJ_2^{|2|}P^{-1}$. We consider $B=PJ_2^{|2|}P^{-1}+P_fP^{-1}$. Alternatively, we can write B as

$$B=\begin{pmatrix} B_{11} & B_{12}\\ B_{21} & B_{22}\end{pmatrix}, \tag{23}$$

where

$$\begin{aligned}
B_{11}&=\frac{\dot S}{S}-\frac{\dot L}{L}-\frac{A\beta}{N}-\frac{B\beta\gamma}{N}-\gamma_3-2d_0-\sigma,\\
B_{12}&=\begin{bmatrix}\frac{\beta}{N}S & \frac{\beta}{N}S\end{bmatrix}, \quad B_{21}=\begin{bmatrix}\sigma\\ 0\end{bmatrix},
\end{aligned}$$

$$B_{22} = \begin{bmatrix} \frac{\dot{S}}{S} - \frac{\dot{L}}{L} - A\frac{\beta}{N} - B\gamma\frac{\beta}{N} - \gamma_1 - 2d_0 - \sigma & 0 \\ A\frac{\beta}{N} + B\gamma\frac{\beta}{N} & \frac{\dot{S}}{S} - 2d_0 - \frac{\dot{L}}{L} - \sigma - \gamma_1 \end{bmatrix}.$$

Assume a vector in R^3 denoted by (b_1, b_2, b_3) and $\|\cdot\|$ is its corresponding norm which is defined by

$$2\|b_1, b_2, b_3\| = \max\{\|b_1\|, \|b_2\| + \|b_3\|\}. \tag{24}$$

Followed [28], we take $\ell(B)$ representing the Lozinski measure with respect to the norm (24), we get

$$\begin{aligned} &\ell(B) \leq \sup\{g_i,\ i = 1, 2\} = \sup\{\|B_{12}\| + \ell(B_{11}),\ \|B_{21}\| + \ell(B_{22})\}, \\ &g_i = \|B_{ij}\| + \ell(B_{ii}), \quad \text{for } i \neq j \text{ and } i = 1, 2. \end{aligned} \tag{25}$$

The use of Equation (25) implies

$$g_1 = \|B_{12}\| + \ell(B_{11}) \text{ and } \ g_2 = \|B_{21}\| + \ell(B_{22}), \tag{26}$$

where

$$\begin{aligned} \ell(B_{11}) &= \frac{\dot{S}}{S} - \frac{\dot{L}}{L} - A\frac{\beta}{N} - B\frac{\beta}{N}\gamma - \gamma_3 - 2d_0 - \sigma, \\ \ell(B_{22}) &= \max\left\{\frac{\dot{S}}{S} - \frac{\dot{L}}{L} - \gamma_3 - \gamma_1 - 2d_0, \frac{\dot{S}}{S} - 2d_0 - \frac{\dot{L}}{L} - \sigma - \gamma_1\right\} \\ &= \frac{\dot{S}}{S} - 2d_0 - \frac{\dot{L}}{L} - \min\{\gamma_3, \sigma\} - \gamma_1, \\ \|B_{12}\| &= \frac{\beta}{N}S, \quad \|B_{21}\| = \max\{\sigma, 0\} = \sigma. \end{aligned} \tag{27}$$

Thus, g_1 and g_2 becomes, $g_1 \leq \frac{\dot{S}}{S} - \sigma - \gamma_3 - 2d_0$ and $g_2 \leq \frac{\dot{S}}{S} - \gamma_1 - 2d_0 + \sigma - \min\{\gamma_3, \sigma\}$, which implies that $\ell(B) \leq \left\{\frac{\dot{S}}{S} + \sigma - \min\{\gamma_3, \sigma\} - 2d_0\right\}$. Hence, $-2\mu_0 + \ell(B) \leq \frac{\dot{S}}{S}$. Integrating $\ell(B)$ in $[0, t]$ and then by taking $\lim_{t\to\infty}$, yields

$$\lim_{t\to\infty} \sup\ \sup \frac{1}{t}\int_0^t \ell(B)dt < -2\mu_0. \tag{28}$$

Finally, we obtain

$$\overline{q} = \lim_{t\to\infty} \sup\ \sup \frac{1}{t}\int_0^t \ell(B)dt < 0.$$

Hence, the system which contains only first three equations of the system (1) is stable globally asymptotically around (S_*, L_*, A_*). Also for the remaining taking the limiting system whose solution yields $C(t)$ and $V(t)$ which approaches to C_* and V_*, respectively as $t \to \infty$. ∎

6 Numerical Simulation

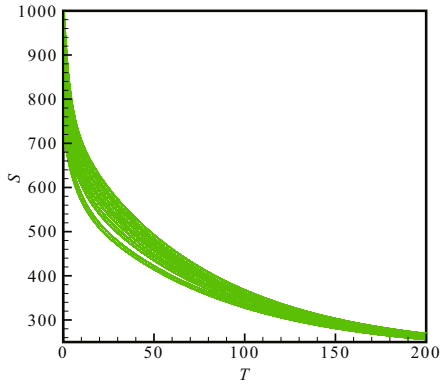
We present the numerical solutions for the verification of theoretical findings of the proposed model (1). We use Runge-Kutta of fourth order method and different values of the parameter

for this purpose of the model (1). The parameters used in the numerical simulation are taken with biologically feasible way given in Table 2.

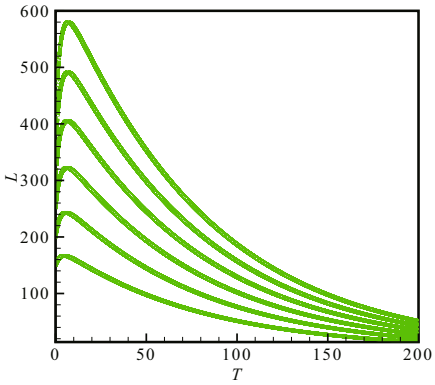
Taking $0-200$ units is the interval of time, while the size of population for $S(t)$, $L(t)$, $A(t)$, $C(t)$, $R(t)$ and $V(t)$ are given in Table 2.

Table 2 Parameter values, weight constants and initial size of compartmental population used in numerical simulation

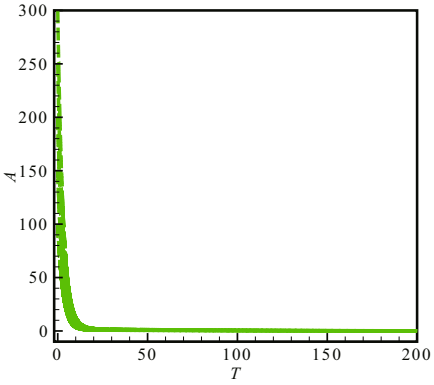
Parameter	parameter description	value	Source
b	new born rate	0.0121	[21]
ξ	new born with unsuccessful vaccination	0.0500	[21]
η	ratio of maternally infected	0.0110	[21]
ϕ	induced rate of waning vaccine	0.1000	[21]
σ	rate of latency to acute	0.0012	[21]
β	hepatitis B transmission rate	0.0950	[21]
γ_1	rate of acute to chronic	0.3300	[21]
γ_2	rate of chronic to immune	0.0090	[21]
γ_3	vaccination rate	0.0200	[21]
d_0	natural mortality rate	0.0121	[21]
d_1	disease-related mortality rate	0.0026	[21]
p	probability of fails individual, who recovers in acute stage	0.8000	Assumed with the help of [21]
A_1	weight constant for $S(t)$	1000.0	[32]
A_2	weight constant for $L(t)$	0.6000	Fitted
A_3	weight constant for $A(t)$	10.000	Fitted
A_4	weight constant for $C(t)$	0.9000	Assumed with the help of [32]
B_1	weight constant for $u_1(t)$	0.4400	Assumed
B_2	weight constant for $u_2(t)$	0.2000	Fitted
B_3	weight constant for $u_3(t)$	1000.0	Assumed
$S(0)$	susceptible	1000.0	[21]
$L(0)$	latent	400.00	[21]
$A(0)$	acute	300.00	[21]
$C(0)$	chronic	200.00	[21]
$R(0)$	recovered	100.00	[21]
$V(0)$	vaccinated	100.00	[21]



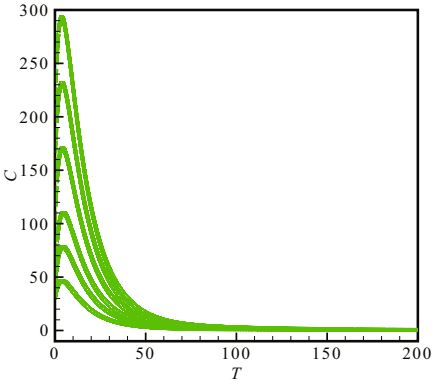
(a) Susceptible individuals



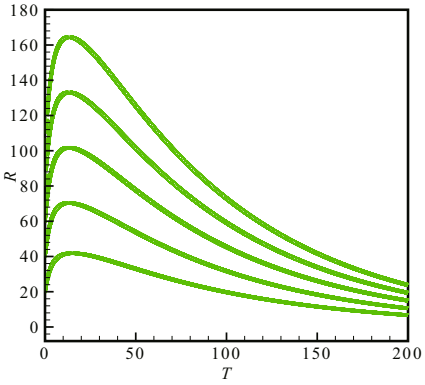
(b) Latent individuals



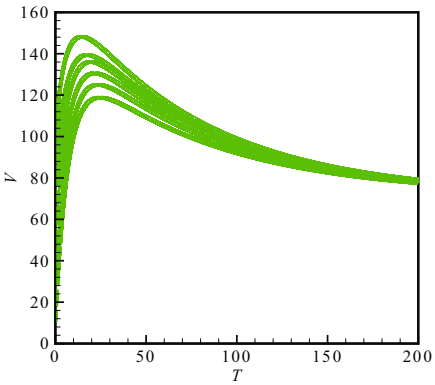
(c) Acutely infected hepatitis B individuals



(d) Chronically infected hepatitis B individuals



(e) Recovered individuals



(f) Vaccinated individuals

Figure 1 Stability curves of (1) with different initial size of population

The simulation part of the study shows that the susceptible population will usually exist. Similarly there is also always vaccinated individuals, but latent, acutely infected, chronic carrier and recovered vanishes, see Figure 1. The trajectories of $S(t)$, $L(t)$, $A(t)$, carriers $B(t)$, $R(t)$ and $V(t)$ go to the equilibrium points as shown in Figures (1(a))–(1(f)). This proves the stability of the model (1).

7 Local Sensitivity

We perform the local sensitivity of the threshold quantity R_0 to define the relative change of the parameters to the infection transmission. It decides the sturdiness of model prediction to the values of the parameter. Commonly during data collection, the uncertainties as well as the estimation of the parameters value considerably affect the threshold quantity.

Definition 7.1 The normalized sensitivity index of R_0 with respect to Φ is defined by

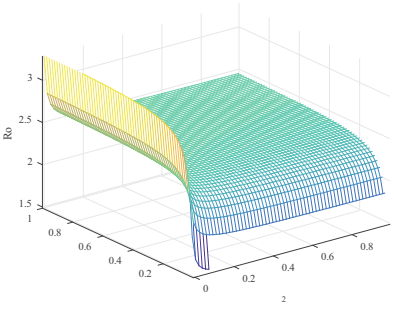
$$S_\Phi = \frac{\Phi}{R_0}\frac{\partial R_0}{\partial \Phi}. \tag{29}$$

We accomplish the sensitivity indices of R_0 to the model parameters, which allow to quantify the comparative variation in R_0 with the variation in a value of the parameter. By the use of these indices, we are able to point out the most risky parameters that extremely affect the threshold quantity R_0.

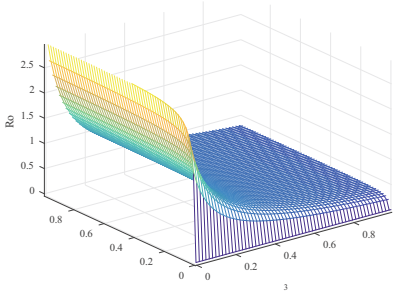
Table 3 represents that σ, β, η, ξ and ϕ have a direct relation with R_0. Which mean that increase or decrease in these values by 10% will increase or decrease R_0 respectively by $10\%, 9.0\%, 5.46\%, 5.46\%$ and 8.13%, see for detail Figure 2. However, on the other side parameters γ_1 and γ_3 have an inverse relation with R_0, which illustrates, that increase in its values by 10% will reduce R_0 by 7.38% and 8.24%, respectively as presented in Figure 2.

Table 3 The sensitive indices of R_0

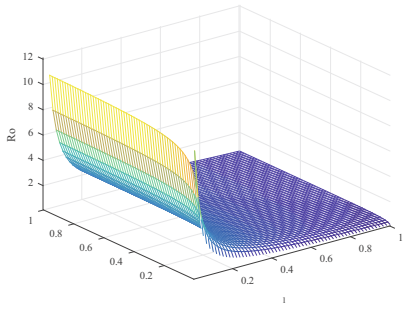
Parameter	Sensitivity index	value
Hepatitis B transmission rate (β)	S_β	+1.0000
Moving rate from L to A (σ)	S_σ	+0.9097
Recovery rate in A (γ_1)	S_{γ_1}	−0.8247
Recovery rate in C (γ_2)	S_{γ_2}	−0.7385
Vaccination (γ_3)	S_{γ_3}	−0.1514
Proportion of vertically infected population (η)	S_η	+0.5460
Birth without successful vaccination (ξ)	S_ξ	+0.5460
waning vaccine induced immunity rate (ϕ)	S_ϕ	+0.8135



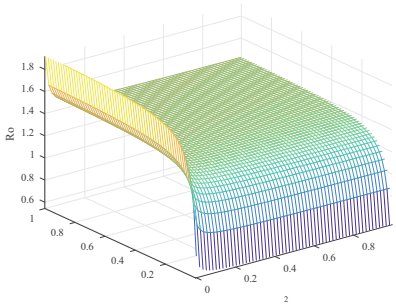
(a) γ_2 and σ verses R_0



(b) γ_3 and σ verses R_0



(c) ϕ and $\gamma_1$verses R_0



(d) The scatter plot of residuals

Figure 2 The plots represent the sensitivity of R_0 w.r.t parameters

In order to eliminate the HBV infection, we need more attention to reduce the transmission rate β. Because this parameter has got the maximum index 1, which demonstrates that the reduction of this parameter by ten percent reduce the value of the R_0 by ten percent. Among these parameters, γ_1 got the second highest index, which is -0.8247, which means that if we increase the value of γ_1 by 10 percent, the value of R_0 will be decrease by 8.24 percent. The sensitivity index of the parameters η, σ, ϕ and ξ is 2.8152 collectively. So 10 percent decrease in these parameters causes 28.152 percent decreases in the value of R_0. Similarly 1.5623 is the sensitivity index of γ_2 and γ_1, therefore if we increase the value of these parameters by 10% will decrease R_0 by 15.632%. Hence, by using this analysis, it is handy to formulate control strategy for the eradication of the HBV infection.

8 Formulation of the Optimal Control Problem

Optimal control theory and calculus of variations are the two techniques which can be used for minimization/maximization problems and many researchers used control theory to make a control strategy for eliminating hepatitis B see, for example, [6, 9, 11, 29–32] and the references cited therein. Control theory applied to HBV infection and related work have been regorously investigated in [33–38]. Based on these studies, we shall focus on optimizing the spreading of infection rate β, whose sensitivity index is 1. The decreases in this rate by 10% will reduce the value of R_0 by 10 percent. The second recovery rate γ_1 of acutely hepatitis B infected

individuals has maximum sensitivity index -0.8247, which has a inverse relation with R_0. So an increase in the recovery rate γ_1 say by 10% reduce R_0 value by 8.247 percent. The index of recovery rate γ_2 of chronic carriers is -0.7385. The increase of the recovery rate γ_2 by say by 10% will also decrease the value of R_0 by 7.385 percent. Similarly the collectively index of η, σ, ϕ and ξ is 2.8152. If we decrease these parameters say by 10%, will decrease R_0 by 28.152%. The parameter γ_3 got the sensitivity index -0.1514, i.e., increase of γ_3 by 10% will effect reduction in the value of R_0 by 1.514 percent.

We coupled all the effect of these parameters parameters β, ξ, η, σ, γ_1, γ_2, γ_3 and ϕ. Growth or decay in the above mentioned parameters can produce the change in the rest parameters. Therefore, on the basis of the above sensitivity indexes, we formulate optimal strategies by introducing the following time dependent control variables.

i) The control measure $u_1(t)$ represents the isolation of non-infected and infected populations. The role of this control is to reduce the hepatitis B transmission rate β.

ii) The control variable $u_2(t)$ represents the control variable treatment of hepatitis B infected individuals. Through this control variable, we want to reduce the number of infected individuals.

iii) $u_3(t)$ represents the control measure vaccination of hepatitis B, i.e., through this control variable, we want to maximize vaccinated population.

Thus, the use of these three variables our control problem become the modified version of the system (1) given by

$$\begin{aligned}
\frac{dS(t)}{dt} =& \xi b(1-\eta C(t))N + \phi V(t) - \frac{\beta S(t)A(t)}{N}(1-u_1(t)) - \frac{\gamma\beta S(t)C(t)}{N}(1-u_1(t)) \\
& - (\gamma_3 + d_0 + u_3(t))S(t), \quad S(0) > 0, \\
\frac{dL(t)}{dt} =& \frac{\beta}{N}A(t)S(t)(1-u_1(t)) + \frac{\beta}{N}\gamma C(t)S(t)(1-u_1(t)) - (d_0+\sigma)L(t) \\
& - (u_2(t)+u_3(t))L(t), \quad L(0) \geq 0, \\
\frac{dA(t)}{dt} =& \sigma L(t) - (d_0 + \gamma_1 + u_2(t) + u_3(t))A(t), \quad A(0) \geq 0, \\
\frac{dC(t)}{dt} =& \xi b\eta C(t)N + \gamma_1 pA(t) - (d_1 + \gamma_2 + u_2(t) + d_0 + u_3(t))C(t), \quad C(0) \geq 0, \\
\frac{dR(t)}{dt} =& \gamma_2 C(t) + (1-p)\gamma_1 A(t) - d_0 R(t) + (L(t) + A(t) + C(t))u_2(t), \quad R(0) \geq 0, \\
\frac{dV(t)}{dt} =& (1-\xi)Nb + \gamma_3 S(t) - (d_0+\phi)V(t) + (S(t)+L(t))u_3(t) \\
& + (A(t)+C(t))u_3(t), \quad V(0) \geq 0.
\end{aligned} \tag{30}$$

The goal of the control strategies is to reduce the acute, chronic and latent population; and the associated cost of $u_1(t)$, $u_2(t)$ and $u_3(t)$. We will assume that the control variables are Lebesgue measurable and bounded. Thus, the objective functional becomes

$$\begin{aligned}
J(u_1,u_2,u_3) = \int_0^{t_f} \Big[& A_1 S(t) + A_2 L(t) + A_3 A(t) + A_4 C(t) \\
& + \frac{1}{2}\Big(B_1 u_1^2(t) + B_2 u_2^2(t) + B_3 u_3^2(t)\Big)\Big] dt,
\end{aligned} \tag{31}$$

subject to the proposed model (30). In the objective functional (31), A_1, A_2, A_3 and A_4 represent the weight constants of the susceptible individuals, latent individuals, acute and carrier population, respectively. The constants B_1, B_2 and B_3 represent the weight constants associated to the controls. More preciously these constants represent the weight constants for isolation, treatment and vaccination, respectively. The terms $\frac{1}{2}B_1u_1^2(t)$, $\frac{1}{2}B_2u_2^2(t)$ and $\frac{1}{2}B_3u_1^3(t)$ represents cost of disease intervention. The cost related with strategy $u_1(t)$ produces due to the cost of isolation of infected and non-infected individuals. The cost associated to the control strategy $u_2(t)$ produces due to medication of infected individuals. The regarding strategy $u_3(t)$ is the cost of vaccination of hepatitis B.

Our goal here is to decrease the size of susceptible, latent, acute and chronic population, and to increase the number of recovered individuals and vaccinated population by using the three time dependent control variables $u_i(t),\ i = 1, 2, 3$. We find the control function, such that

$$J(u_1^*, u_2^*, u_3^*) = \min\{J(u_1, u_2, u_3), u_1, u_2, u_3 \in U\} \tag{32}$$

subject to the proposed model (30), where the control set is defined as,

$$U = \left\{(u_1, u_2, u_3)|u_i(t) \text{ are Lebesgue measurable on } [0, 1], 1 \geq u_i(t) \geq 0, i = 1, 2, 3\right\}. \tag{33}$$

Before moving further, we need to show that such control measures exist.

8.1 Existence of Solution

In this subsection, we will show that a solution of the control problem (30) exist. For nonnegative subsidiary conditions and bounded Lebesgue measurable controls functions, there exist positive bounded solution to the state system[39]. To show the existence of solution of the proposed control problem (30), we investigate the following result.

Theorem 8.1 *There exist a set of control measures $u^* = (u_1^*, u_2^*, u_3^*) \in U$, such that*

$$J(u_1^*, u_2^*, u_3^*) = \min J(u_1, u_2, u_3),$$

subject to the control system (30).

Proof Clearly the following holds

i) The control measures $u_i(t)$ for $i = 1, 2, 3$ and the state variables (S, L, A, C, R, V) are nonnegative.

ii) The control set U is convex and closed.

iii) Boundedness of the optimal system assures the compactness.

iv) The integrand $A_1S(t) + A_2L(t) + A_3A(t) + A_4C(t) + \frac{1}{2}(B_1u_1^2 + B_2 2u_2^2 + B_3u_3^2)$ in (31) is convex on U, which completes the proof. ∎

8.2 Optimality Condition

To characterize the optimal solution for (30), let us define the Lagrangian and the Hamiltonian associated with our optimal problem. Thus, the Lagrangian is given by

$$\begin{aligned} L(S,L,A,C,u_1,u_2,u_3) &= A_1S(t)+A_2L(t)+A_3A(t)+A_4C(t)\\ &\quad+\frac{1}{2}(B_1u_1^2(t)+B_2u_2^2(t)+B_3u_2^3(t)). \end{aligned} \tag{34}$$

For the purpose of minimal value of the Lagrangian, we define H (Hamiltonian) for (30) as

$$H(x,u,\lambda)=L(x,u)+\lambda\cdot F(x,u), \tag{35}$$

where

$$\begin{aligned} &x=(S,L,A,C),\quad u=(u_1,u_2,u_3),\quad \lambda=(\lambda_1,\lambda_2,\cdots,\lambda_6),\\ &F_1(x,u)=\phi V(t)+b\xi N(1-\eta C(t))-\left(\frac{\beta}{N}S(t)A(t)+\frac{\beta}{N}\gamma S(t)C(t)\right)(1-u_1(t))\\ &\qquad-(\gamma_3+d_0+u_3(t))S(t),\\ &F_2(x,u)=\left(\frac{\beta}{N}A(t)S(t)+\frac{\beta\gamma S(t)C(t)}{N}\right)(1-u_1(t))-(d_0+\sigma)L(t)\\ &\qquad-(u_2(t)+u_3(t))L(t),\\ &F_3(x,u)=\sigma L(t)-(\gamma_1+d_0+u_2(t)+u_3(t))A(t),\\ &F_4(x,u)=\xi b\eta C(t)N+\gamma_1pA(t)-(d_1+\gamma_2+d_0+u_2(t)+u_3(t))C(t),\\ &F_5(x,u)=\gamma_2C(t)+(1-p)\gamma_1A(t)-d_0R(t)+(L(t)+A(t)+C(t))u_2(t),\\ &F_6(x,u)=bN(1-\xi)+\gamma_3S(t)-(d_0+\phi)V(t)+(S(t)+L(t))u_3(t)\\ &\qquad+(A(t)+C(t))u_3(t), \end{aligned} \tag{36}$$

and $F(x,u)=(F_1,F_2,\cdots,F_6)(x,u)$. For the optimal solution to the developed control problem, we will prefer to use Pontryagin'n Maximum Principle[28]: If (x^*,u^*) is an optimal solution to (30) with u^* being essentially bounded, then there exists a non-trivial vector function λ, such that the Hamiltonian system

$$\begin{cases} \dfrac{dx^*(t)}{dt}=\dfrac{\partial H}{\partial\lambda}(x^*(t),u^*(t),\lambda(t)),\\ \dfrac{d\lambda(t)}{dt}=-\dfrac{\partial H}{\partial x}(x^*(t),u^*(t),\lambda(t)),\\ 0=\dfrac{\partial H}{\partial u}(x^*(t),u^*(t),\lambda(t)), \end{cases} \tag{37}$$

the maximality condition

$$H(x^*(t),u^*(t),\lambda(t))=\max_{u_1,u_2,u_3\in[0,1]}H(x^*(t),u_1,u_2,u_3,\lambda(t)); \tag{38}$$

and the transversality condition

$$\lambda(t_f)=0 \tag{39}$$

hold.

Theorem 8.2 *Let S^*, L^*, A^*, C^*, R^* and V^* be optimal states solutions associated to essentially bounded optimal controls (u_1^*, u_2^*, u_3^*) for the optimal control problem* (30)*. Then there exist adjoint variables $\lambda_i(t)$, $i = 1, 2, \cdots, 6$, satisfying*

$$\begin{aligned}
\frac{d\lambda_1(t)}{dt} &= (\lambda_1(t) - \lambda_2(t))\left(\frac{\beta A^* + \gamma\beta C^*}{N}(1 - u_1(t))\right) + \lambda_1(t)(d_0 + \gamma_3 + u_3(t)) - A_1 \\
&\quad - \lambda_6(t)(\gamma_3 + u_3(t)), \\
\frac{d\lambda_2(t)}{dt} &= \lambda_2(t)(\sigma + d_0 + u_2(t) + u_3(t)) - \sigma\lambda_3(t) - \lambda_5(t)u_2(t) - \lambda_6(t)u_3(t) - A_2, \\
\frac{d\lambda_3(t)}{dt} &= (\lambda_1(t) - \lambda_2(t))\left(\frac{\beta S^*}{N}(1 - u_1(t))\right) + \lambda_3(t)(d_0 + \gamma_1 + u_2(t) + u_3(t)) \\
&\quad - \lambda_4(t)p\gamma_1 - \lambda_5(t)((1-p)\gamma_1 + u_2(t)) - \lambda_6(t)u_3(t) - A_3, \\
\frac{d\lambda_4(t)}{dt} &= -A_4 + (\lambda_1(t) - \lambda_2(t))\left(\frac{\gamma\beta S^*}{N}(1 - u_1(t))\right) + \lambda_1(t)b\xi\eta N \\
&\quad - \lambda_4(t)(b\xi\eta N - (d_0 + d_1 + \gamma_2 + u_2(t) + u_3(t))) - \lambda_5 u_2(t) - \lambda_6(t)u_3(t), \\
\frac{d\lambda_5(t)}{dt} &= d_0\lambda_5(t), \\
\frac{d\lambda_6(t)}{dt} &= \lambda_1(t)\phi + (d_0 + \phi)\lambda_6(t),
\end{aligned} \tag{40}$$

with transversality conditions

$$\lambda_i(t_f) = 0 \quad \textit{for} \quad i = 1, 2, \cdots, 6. \tag{41}$$

Furthermore, the optimal controls variable $u_1^*(t)$, $u_2^*(t)$ and $u_3^*(t)$ are given by

$$\begin{aligned}
u_1^* &= \max\left\{\min\left\{\frac{(\beta S^* A^* + \gamma\beta S^* C^*)(\lambda_2(t) - \lambda_1(t))}{NB_1}, 1\right\}, 0\right\}, \\
u_2^* &= \max\left\{\min\left\{\frac{(\lambda_2(t) - \lambda_5(t))L^* + (\lambda_3(t) - \lambda_5(t))A^* + (\lambda_4(t) - \lambda_5(t))C^*}{B_2}, 1\right\}, 0\right\}, \\
u_3^* &= \max\left\{\min\left\{\frac{(\lambda_1(t)S^* + \lambda_2(t)L^* + \lambda_3(t)A^* + \lambda_4(t)C^* - \lambda_6(t))(S^* + L^* + A^* + C^*)}{B_3}, 1\right\}, 0\right\}.
\end{aligned}$$

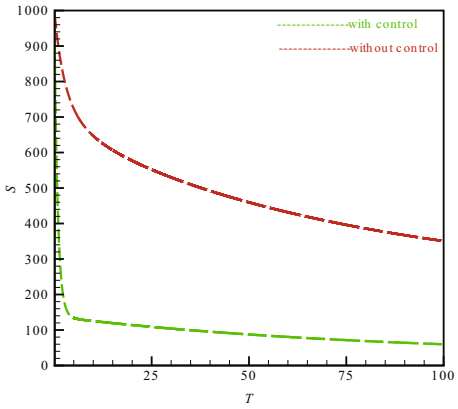
Proof System (40) is direct comes from applying adjoint equation of the Pontryagin Maximum Principle to our problem, that is, from the 2nd equation in (37) with the Hamiltonian H defined by (34)–(36), while conditions (41) is a direct consequence of the transversality condition (39). To obtain u_1^*, u_2^* and u_3^*, we differentiate the Hamiltonian with respect to control measures, then we solve the system $\frac{\partial H}{\partial u_1} = 0$, $\frac{\partial H}{\partial u_2} = 0$ and $\frac{\partial H}{\partial u_3} = 0$ (necessary optimality conditions for the finite dimension optimization problem on the right-hand side of (38), when one restrict himself to the interior $(0, 1) \times (0, 1)$ of the optimization region). Lastly, by using the maximality condition (38), we obtain the optimal control measures u_1^*, u_2^* and u_3^*, which completes the proof. ∎

We found the optimal state and control variables by solving numerically the optimality system, which contains the state system (30) and the adjoint system (40), boundary conditions (41)

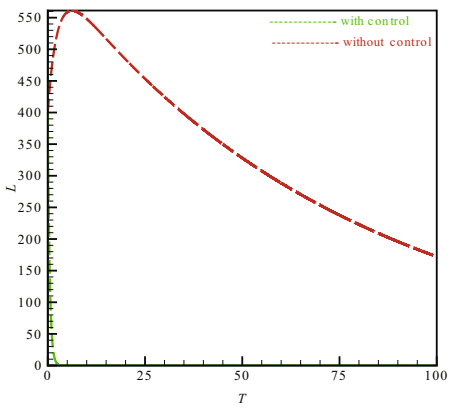
and (41), together with the characterization of the optimal values of the controls (u_1^*, u_2^*, u_3^*). In addition, the Hessian matrix of the Hamiltonian with respect to u_1, u_2 and u_3 should be positive semidefinite, describing the fact that we are considering a minimization problem.

9 Numerical Analysis of the Optimal Problem

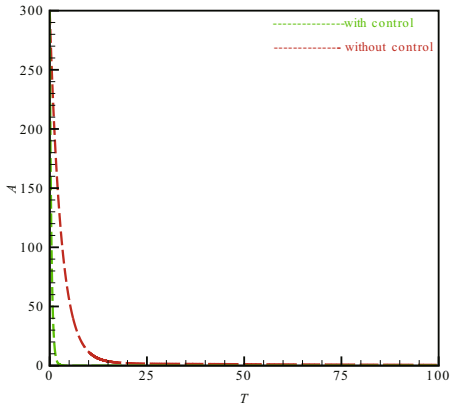
To simulate the control problem, we intend to use Runge-Kutta procedure of order four. More precisely, we wish to solve the state system (30) by using the Runge-Kutta scheme of order four with initial conditions (41) forward in time $[0, 100]$, and subsequently solving the adjoint system (40) by the backward Runge-Kutta of order four in the same interval of time with the help of the transversality conditions (41) and the solution of the state system. For simulation purposes, the following parameter values were chosen are given in Table 2. The results presented in Figures 3–5 were obtained. Figure 3 represents the graphs of susceptible population, latent population, acute hepatitis B infected population and chronically infected hepatitis B population with and without (optimal) control. The simulations illustrate clearly our objective in applying the controls: To reduce the number of susceptible, latent, acute and chronically infected with hepatitis B population, and to increase the number of recovered individuals and vaccinated population. Figure 3(a) represents the graph of susceptible individuals with and without (optimal) control. Similarly, Figures 3(b)–(d) represents the graph of latent, acute, chronically infected individuals with and without (optimal) control, while Figure 3 represents the graphs of recovered and vaccinated individuals with and without (optimal) control. Furthermore, Figure 3 represents the dynamic of the optimal control variables. Clearly, the difference between the two cases is visible.



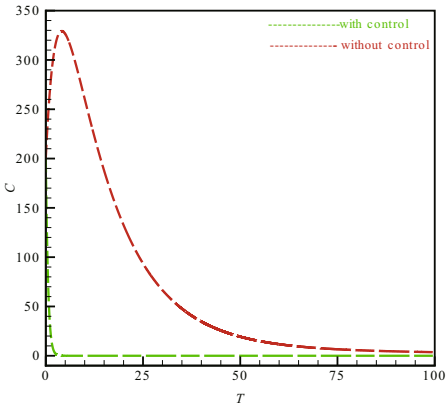
(a) Susceptible population



(b) Latent population

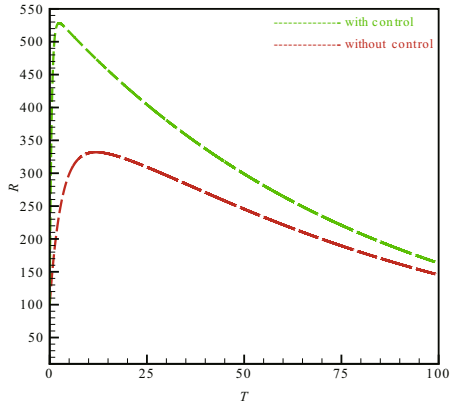


(c) Acute population

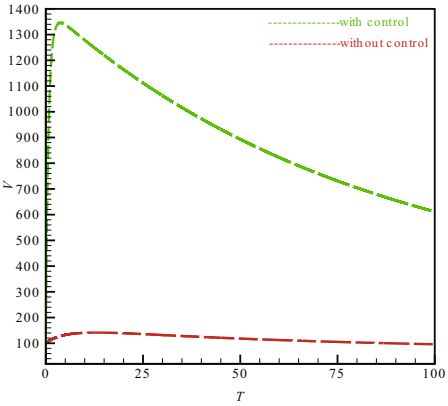


(d) Chronic population

Figure 3 The time dynamics of the compartmental population model (1) with and without control

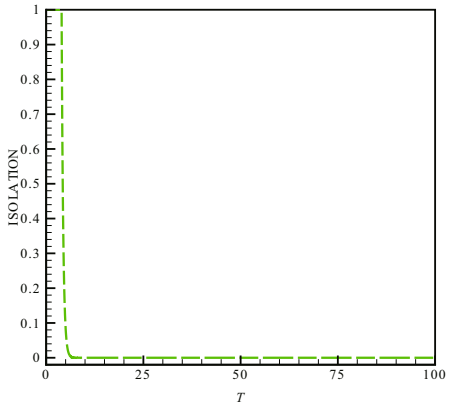


(a) Recovered population

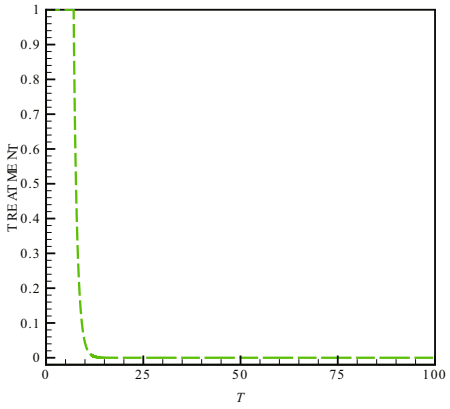


(b) Vaccinated population

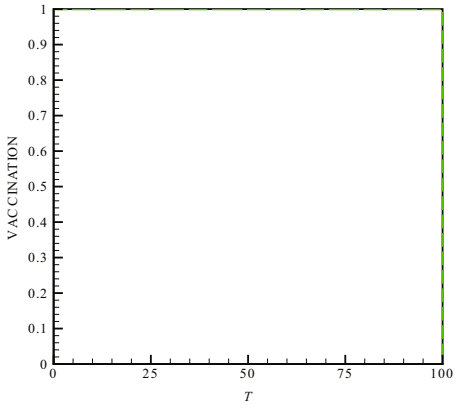
Figure 4 The time dynamics of the recovered and vaccinated population with and without control



(a) Optimal control variable isolation $u_1(t)$



(b) Optimal control variable treatment $u_2(t)$



(c) Optimal control variable vaccination $u_3(t)$

Figure 5 The time dynamics of the optimal control variables

10 Discussion and Conclusion

In this section, the discussion and concluding remarks are presented. First, the discussion of the numerical simulation is presented. The control variables $u_1(t)$, $u_2(t)$ and $u_3(t)$ reduces the transmission rate β, the moving rate σ of latent individuals to acute class, the proportion of parentally infected individuals η, the birth rate without successful vaccination ξ and the waning vaccine induced immunity rate ϕ. Which causes decrease in the transmission and consequently decrease the susceptible individual $S(t)$, the latent individual $L(t)$, the acute hepatitis B individuals $A(t)$ and the chronic carrier individuals $C(t)$ as shown in Figures 3 (a)–(d). While causes increase in the non-infected individuals, which consequently increase the recovered individuals $R(t)$ and $V(t)$ as shown in Figures 4 (a)–(b). The graph of susceptible population approaches to a small number due to optimal control $u_1(t)$ and $u_2(t)$ as shown

in Figure 3 (a). Similarly the graph of latent population, acute infected and chronic carrier population approaches to a small number due to optimal control shown in Figures 3 (b)–(d). While Figures 4 (a)–(b) shows that the recovered and vaccinated individuals are approaches to a large number in case of with optimal control.

In this work, we studied hepatitis B epidemic model with nonlinear incidence. We studied different mathematical properties of boundedness and positivity to show the biological feasibility. We found reproduction number and discussed the sensitivity analysis. We also used the optimization theory and developed a control strategy on the basis of normalized sensitive index to eliminate hepatitis B from the population. By using the normalized sensitivity index, we investigated the most sensitive parameters and then developed the control strategy. For this purpose, we used three time-dependent control measures, the isolation of non-infected and infected individuals, $u_1(t)$, the treatment, $u_2(t)$ and the vaccination, $u_3(t)$. Once, we formulated the optimal control problem, then proved the existence and characterize the optimality condition using the Pontryaginn Maximum Principle. Finally, the numerical simulation of the optimal problem are presented to support the analytical work.

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