Mathematical Modeling of Transmission Dynamics and Optimal Control of Isolation, Vaccination and Treatment for Hepatitis B Virus

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Abstract. In this paper we formulate an SEICR (Susceptible- Exposed- Infective- Carrier- Recovered) model of Hepatitis B Virus (HBV) disease transmission with constant recruitment. The threshold parameter $R_0 < 1$, known as the Basic Reproduction Number was found.

This model has two equilibria, disease-free equilibrium and endemic equilibrium. The Sensitivity analysis of the model was done, three time-varying control variables are considered and a control strategy for the minimization of infected individuals with latent, infectious and chronic HBV was developed.

Keywords: *Stability Analysis, Basic Reproduction Number, Jacobian Matrix, Sensitivity Analysis*
Mathematics Subject Classifications: 03C65

1. Introduction:

Hepatitis B is a life-threatening liver infection which is caused by the hepatitis B virus. It is a major global health problem [8]. It can cause chronic liver disease and chronic infection and puts people at high risk of death from cirrhosis of the liver and liver cancer [16]. Infections of hepatitis B occur only if the virus is able to enter the blood stream and reach the liver. Once in the liver, the virus reproduces and releases large numbers of new Viruses into the blood stream [3]. This infection has two possible phases: (1) acute and (2) chronic, acute hepatitis B infection lasts less than six months. If the disease is acute, the immune system is usually able to clear the virus from your body, and one will recover completely within a few months. Chronic hepatitis B infection lasts six months or longer most infants infected with HBV at birth and many children infected between 1 and 6 years of age become chronically infected [16]. About two-thirds of people with chronic HBV infection are chronic carriers. These people do not develop symptoms, even though they harbor the virus and can transmit it to other people. The remaining one-third develop active hepatitis, a disease of the liver that can be very serious [8].

In this work, we study the dynamics of hepatitis B virus (HBV) infection under administration of vaccination, isolation of the infected individual and treatment, where HBV infection is transmitted in two ways through vertical transmission and horizontal transmission. The horizontal transmission is reduced through the isolation of the infected individual and the administration of vaccination to those susceptible individuals, the vertical transmission gets reduced through the administration of treatment to infected individuals and isolation of the infected individual; therefore, the vaccine and the treatment play different roles in controlling the HBV [2]. In this work we analyze and apply optimal control to determine the possible impacts of isolation of the

infected individual, vaccination to susceptible individuals and treatment to infected individuals. Some numerical simulations of the model are also given to illustrate the results and to find optimal strategies in controlling HBV infection. Sensitivity analysis also was carried out to know the parameter that has greater impact on the spread of the disease.

The work is organized as follows. We proposed an HBV infection model with isolation, vaccination and treatment, we analyzed the qualitative property of the model also we considered the optimal analysis of the model and finally we considered some numerical experiments under special choice of parameter values. The paper will be finished with a brief discussion and conclusion.

2. Model Formation

The model is an heterosexually active population. The disease that guides the modeling is gonorrhea and, consequently, infective recover after treatment. It was assumed that the population is genetically and behaviorally homogeneous except for the gender of individuals in the population. The model used is a Susceptible-Latent-Infective-Carrier-Recovered-Vaccine model, that is, a homogeneously mixing SLICRV model. where S , L , I , C , R , and V denotes the proportion of individuals at the stage of susceptible, latent, acute, carrier, recovery, and vaccinated to HBV in the total population, respectively. t is time, λ is the force of HBV infection, σ is the proportion of perinatal infection, α is the rate at which individuals leave the latent class, γ is the rates at which individuals leave the acute class, δ is the recovery rate of carriers, ρ is the probability for an individual suffering from acute HBV infection to become a chronic carrier, ν is the rate of successful vaccination, ω is proportion of births with successful vaccination, ϕ is the rate of waning vaccine-induced immunity, b is the birth rate, μ is the natural mortality rate. In these models, all of the parameters are assumed to be constant.

Model Equation

We have the following non-linear system of differential equations,

$$\left. \begin{aligned} \frac{dS}{dt} &= b(1-\omega)(1-\sigma C) + \phi R - (\mu + \lambda + \nu)S \\ \frac{dL}{dt} &= \lambda S - (\mu + \alpha)L \\ \frac{dI}{dt} &= \alpha L - (\mu + \gamma)I \\ \frac{dC}{dt} &= b\sigma(1-\omega)C + \rho\gamma I - (\mu + \delta + \phi)C \\ \frac{dR}{dt} &= (1-\rho)\gamma I + (\delta + \phi)C - (\mu + \phi)R - \psi V \\ \frac{dV}{dt} &= b\omega + \nu S + \psi V - \mu V \end{aligned} \right\} \quad (1)$$

Table(1): Descriptions of Parameters

Parameters	Definitions
b	Birth rate
α	Progression rate from Latent
ω	Proportion of birth with successful vaccinated
λ	Force of infection
μ	Natural death rate
σ	Proportion of perinatal infection
ρ	Probability of acute infected becoming chronic
γ	Progression rate from acute infected
δ	Recovery rate
ϕ	Waning rate
ν	successful vaccination

Table(2): Description of Variables

Variables	Definitions
S	Susceptible Individual
L	Latent Individual
I	Infected Individual
C	Carrier Individual
R	Recovered Individual
V	Vaccinated Individual

Model Analysis

Positivity of Solution

Similar model (1) model human population, It is crucial to note that model (1) will be analyzed in a feasible region D, given by $D = \{(S, L, I, C, R, V) \in \mathbb{R}_+^6 : S + L + I + C + R + V = 1\}$. Hence, all state variable S, L, I, C, R, V are non-negative then it is epidemiologically and mathematically well posed

Existence of Disease Free Equilibrium (DFE)

The model in (1) has disease free equilibrium given by

$$\varepsilon_0 = (S_0, L_0, I_0, C_0, R_0, V_0) = \left(\frac{b(1-\omega)}{\mu+\nu}, 0, 0, 0, 0, \frac{b(\mu\omega+\nu)}{(\mu+\nu)(\mu-\psi)} \right) \quad (2)$$

Existence of Endemic Equilibrium Point (EEP)

And now solve model (1) simultaneously to get the endemic equilibrium point, it given below;

$$\left. \begin{aligned} S^{**} &= \frac{K_2 K_3 K_4}{\beta \alpha K_1} & I^{**} &= \frac{\mu K_2 K_5 S^{**} (R_0 - 1)}{\alpha K_7 K_8 \beta S^{**}} & L^{**} &= \frac{\mu K_4 K_5 K_6 S^{**} (R_0 - 1)}{\alpha K_7 K_8 \beta S^{**}} \\ C^{**} &= \frac{\mu \beta \rho \gamma K_5 K_9 S^{**2} (R_0 - 1)}{K_7 K_8 \beta S^{**}} & R^{**} &= \frac{\mu \beta (1-\rho) \gamma K_4 \psi K_5 S^{**2} (R_0 - 1)}{K_7 K_8 \beta S^{**}} & V^{**} &= \frac{\mu(1-\omega) + \nu S}{K_8} \end{aligned} \right\} \quad (3)$$

Where

$$\begin{aligned} K_1 &= \mu + \delta + \phi + \rho\gamma - b\sigma(1-\omega), & K_2 &= \mu + \delta + \phi - b\sigma(1-\omega), & K_3 &= \alpha + \mu & K_4 &= \mu + \gamma, & K_9 &= \mu + \delta \\ K_5 &= \mu + \nu + \psi & K_6 &= \delta + \mu + \phi & K_8 &= \mu + \psi & K_7 &= \mu + \delta + \phi + \rho\gamma - b\sigma(1-\omega) + b\sigma(1-\omega) \end{aligned}$$

Basic Reproduction Number (R_0)

Using next generation matrix [15],

$$F = \begin{pmatrix} 0 & \frac{(1-\omega)\beta B}{\mu+\nu} & \frac{(1-\omega)\beta B}{\mu+\nu} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ at DFE}$$

$$V = \begin{pmatrix} \mu+\alpha & 0 & b\sigma(1-\omega) & 0 \\ -\alpha & \mu+\gamma & 0 & 0 \\ 0 & -\rho\gamma & (\mu+\delta+\phi)-b\sigma(1-\omega) & 0 \\ 0 & -(1-\rho)\gamma & -(\delta+\phi) & \mu+\phi \end{pmatrix}$$

Thus;

$$R_0 = \frac{\beta b(1-\omega)\alpha[(b\sigma(\omega-1)+\mu+\phi+\delta)+1]}{(\mu+\nu)(\mu+\alpha)(\mu+\gamma)(b\sigma(\omega-1)+\mu+\phi+\delta)} \quad (4)$$

The threshold quantity R_0 is the basic reproduction number of the system (1) for Hepatitis B infection. It is the average number of new secondary infections generated by a single infected individual in his or her infectious period. [9].

Local Stability of the DFE

Theorem 3: The disease free equilibrium of the model (1) is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: To determine the local stability of E_0 , the following Jacobian matrix is computed corresponding to equilibrium point E_0 . Considering the local stability of the disease free equilibrium

at $\left(\frac{b(1-\omega)}{\mu+\nu}, 0, 0, 0, 0, \frac{b(\mu\omega+\nu)}{(\mu+\nu)(\mu-\psi)}\right)$ We have

$$J_G = \begin{pmatrix} -(\mu + \beta(I+C) + \nu) & 0 & -\beta S & -\beta S - b(1-\omega)\sigma & \phi & 0 \\ \beta(I+C) & -(\mu + \alpha) & \beta S & \beta S & 0 & 0 \\ 0 & \alpha & (\mu + \gamma) & 0 & 0 & 0 \\ 0 & 0 & \rho\gamma & b(1-\omega)\sigma - (\mu + \delta + \phi) & 0 & 0 \\ 0 & 0 & (1-\rho)\gamma & (\delta + \phi) & -(\mu + \phi) & -\psi \\ \nu & 0 & 0 & 0 & 0 & \psi - \mu \end{pmatrix} \quad (5)$$

The characteristics polynomial of the above matrix is given by

$$B_5 \lambda^5 + B_4 \lambda^4 + B_3 \lambda^3 + B_2 \lambda^2 + B_1 \lambda + B_0 = 0 \quad (6)$$

Thus by Routh – Hurwitz criteria, E_0 is locally asymptotically stable as it can be seen for

$B_1 > 0, B_2 > 0, B_3 > 0, B_4 > 0, B_5 > 0, B_1 B_3 - B_3 > 0$ and $B_1 B_2 B_3 - B_3^2 - B_1^2 B_4 > 0$ Thus, using $B_0 > 0$

$$B_0 = \frac{\beta b(1-\omega)\alpha[(b\sigma(\omega-1) + \mu + \phi + \delta) + 1]}{(\mu+\nu)(\mu+\alpha)(\mu+\gamma)(b\sigma(\omega-1) + \mu + \phi + \delta)} < 1 \quad (7)$$

Hence

$$R_0 < 1$$

The result from Routh Hurwitz criterion shows that, alleigen-values of the polynomial are negative which shows that the disease free equilibrium is locally asymptotically stable.

Sensitivity Analysis

This section examines changing effects of the model parameters with respect to basic reproduction number, R_0 , of the model (1). To determine how changes in parameters affect the transmission and spread of the disease with recovered, a sensitivity analysis of model (1) is carried out in the sense of [9],[13].

Definition 1. The normalized forward-sensitivity index of a variable, v , depends differentiable on a parameter, p , is defined as:

$$\gamma_p^v = \frac{\partial v}{\partial p} \times \frac{p}{v} \quad (8)$$

In particular, sensi parameter. For example, using the above equation, we obtain:

Parameter	Sign
B	Positive
B	Positive
Ω	Negative
A	Positive
Σ	Positive
M	Negative
Φ	Positive
Δ	Positive
Γ	Negative

The positive sign of S.I of R_0 to the model parameters shows that an increase (or decrease) in the value of each of the parameter in this case will lead to an increases (or decrease) in R_0 of the model (1) and asymptotically results into persistence (or elimination) of the disease in the community . For instance $\gamma \frac{R_0}{\beta} = 1$ means that increasing (or decreasing) by β 10% increases (or decreases) R_0 by 10%. On the contrary, the negative sign of R_0 to the model parameters indicates that an increase (or decrease) in the value of each of the parameter in this case leads to a corresponding decrease (or increases) on R_0 of the model (1). Hence, with sensitivity analysis, one can get insight on the appropriate intervention strategies to prevent and control the spread of the disease described by model (1).

Optimal control formulation

In this part, we find optimal control strategies that minimize the number of infected individuals with latent, acute and carrier of HBV represented by $L(t)$, $I(t)$ and $C(t)$, respectively. Three time-varying control variables $u_1(t)$, $u_2(t)$ and $u_3(t)$ which represent the level of effort of isolation of infected and non- infected individuals, vaccination and treatment of infected individuals, respectively are incorporated into Model (1) so that the dynamics of controlled HBV transmission is given by

$$\begin{aligned}\frac{dS(t)}{dt} &= b(1-\omega)(1-\sigma C(t)) + \phi R(t) - (1-u_1(t))\beta(I(t)+C(t))S(t) - (\mu+u_2(t))S(t) \\ \frac{dL(t)}{dt} &= (1-u_1(t))\beta(I(t)+C(t))S(t) - (\mu+\alpha)L(t) \\ \frac{dI(t)}{dt} &= \alpha L(t) - (\mu+\gamma+u_3(t))I(t) \\ \frac{dC(t)}{dt} &= b(1-\omega)(1-\sigma)C(t) + \rho I(t) - (\mu+\delta+\phi+u_3(t))C(t) \\ \frac{dR(t)}{dt} &= (1-\rho)I(t) + (\delta+\phi)C(t) - (\mu+\phi)R(t) - \psi V(t) + u_3(t)(I(t)+C(t)) \\ \frac{dV(t)}{dt} &= b\omega + u_2(t)S(t) + \psi V(t) - \mu V(t)\end{aligned}\tag{9}$$

subject to the initial conditions:

$$S(0) = S_0, L(0) = L_0, I(0) = I_0, C(0) = C_0, R(0) = R_0, V(0) = V_0.\tag{10}$$

In order to formulate the optimal control problem, we specify our objective functional as presented in the next subsection.

Objective functional

We define our objective functional as Mimimize

$$J(u_1, u_2, u_3) = \int_0^T L(L(t), I(t), C(t), u_1(t), u_2(t), u_3(t)) dt\tag{11}$$

subject to the state equation (9) together with the initial conditions (10).

In the objective functional given by Equation (11), L is the Lagrangian defined as

$$L = A_1 L(t) + A_2 I(t) + A_3 C(t) + \frac{1}{2} \sum_{i=1}^3 B_i u_i^2\tag{12}$$

are the weight constants of latent individuals, acute-infected individuals and chronic (carrier) infected individuals, respectively. Also, B_1 , B_2 and B_3 are the weight constants, which represent isolation of infected and non-infected individuals, vaccination and treatment, respectively. The $\frac{1}{2}B_1 u^2$, $\frac{1}{2}B_2 u^2$ and $\frac{1}{2}B_3 u^2$ terms account for the relative cost associated to isolation, vaccination and treatment, respectively over the time interval $[0, T]$, while T is the final time. Our goal here is to obtain an optimal control pair (u_1, u_2, u_3) such that

$$J(u_1, u_2, u_3) = \min \{ J(u_1, u_2, u_3) \in U \} \quad (13)$$

subject to the state equation, Model (9) with the control set given by

$$U = \{ (u_1, u_2, u_3) : u_i \text{ is Lebesgue measurable on } [0, T], 0 \leq u_i \leq 1, i = 1, 2, 3 \}.$$

Existence of an optimal control

In this subsection, we study the sufficient conditions that guarantee the existence of a solution to the optimal control problem presented by Equations (1) and (2).

Theorem 1. Consider the optimal control problem together with the state Equation (1). There exists an optimal control set $u^* = (u_1^*, u_2^*, u_3^*)$ with a corresponding solution $(S^*, L^*, I^*, C^*, R^*, V^*)$ to the Model (1) that minimizes $J(u_1, u_2, u_3)$ over U .

Proof. To prove this Theorem, we use Theorem 4.1 of Chapter III in [8]. to check that the following conditions are satisfied:

- C1. The set of solution to Equation (1) together with the initial condition (2) and the corresponding control function in U is non-empty.
- C2. The control set U is convex and closed.
- C3. The state system can be written as a linear function of the control variables with coefficient dependent on time and state variables.
- C4. The Lagrangian $L(S(t), L(t), I(t), C(t), R(t), V(t), u_1(t), u_2(t), u_3(t))$ in Equation (3) is convex on U .
- C5. There exist constants $\eta_1, \eta_2 > 0$ and $\vartheta > 1$ such that $L(S(t), L(t), I(t), C(t), R(t), V(t), u_1(t), u_2(t), u_3(t))$ is bounded below by $\eta_1 |(u_1, u_2, u_3)| - \eta_2$.

In order to verify C1, we use a result from [18]. Following [15], we re-write Model (9) in the form

$$\dot{Z}(t) = AZ + F(Z) \quad (14)$$

Where,

$$Z = (S(t), L(t), I(t), C(t), R(t), V(t))^T \quad (15)$$

$$A = \begin{pmatrix} -(\mu + u_2(t)) & 0 & 0 & -b\sigma(1-\omega) & \varphi & 0 \\ 0 & -(\mu + \alpha) & 0 & 0 & 0 & 0 \\ 0 & \alpha & -(\mu + \gamma + u_3(t)) & 0 & 0 & 0 \\ 0 & 0 & \rho\gamma & b\sigma(1-\omega) - (\mu + \delta + \phi + u_3(t)) & 0 & 0 \\ 0 & 0 & (1-\rho)\gamma + u_3(t) & \delta + \phi + u_3(t) & -(\mu + \varphi) & -\psi \\ u_2(t) & 0 & 0 & 0 & 0 & \psi - \mu \end{pmatrix}$$

And

$$F(Z) = \begin{pmatrix} b\sigma(1-\omega) - (1-u_1(t))\beta(I(t) + C(t))S(t) \\ (1-u_1(t))\beta(I(t) + C(t))S(t) \\ 0 \\ 0 \\ 0 \\ b\omega \end{pmatrix}$$

The system (15) is nonlinear with bounded coefficients. Setting

$$G(Z) = AZ + F(Z) \quad (16)$$

then $F(Z)$ in Equation (8) satisfies

$$\begin{aligned} |F(Z_1) - F(Z_2)| &\leq (p_1 |S_1(t) - S_2(t)| + p_2 |L_1(t) - L_2(t)| + p_3 |I_1(t) - I_2(t)| + p_4 |C_1(t) \\ &\quad - C_2(t)| + p_5 |R_1(t) - R_2(t)| + p_6 |V_1(t) - V_2(t)|), \\ &\leq p (|S_1(t) - S_2(t)| + |L_1(t) - L_2(t)| + |I_1(t) - I_2(t)| + |C_1(t) - C_2(t)| \\ &\quad + |R_1(t) - R_2(t)| + |V_1(t) - V_2(t)|), \end{aligned} \quad (17)$$

where, $p = \max \{p_1, p_2, p_3, p_4, p_5, p_6\}$ is a positive constant independent of the state variables. Fur- there more,

$$|G(Z_1) - G(Z_2)| \leq p |Z_1 - Z_2|, \quad (18)$$

where $p = p_1 + p_2 + p_3 + p_4 + p_5 + p_6 + \|W\| < \infty$. Thus, it follows that the function $G(Z)$ is uniformly Lipschitz continuous. From the definition of the control variables, one can see that a solution of Model (18) exists. Hence, C1 holds.

The boundedness of the control set U follows directly from definition. Thus, C2 holds. From Equation (1), the state equations are linearly dependent on the controls u_1 , u_2 and u_3 , then C3 is verified. Since the Lagrangian $L(S(t), L(t), I(t), C(t), R(t), V(t), u_1(t), u_2(t), u_3(t))$ is quadratic in the controls, then it is convex. Thus, we have verified C4. Finally, we verify C5 as follows:

There are $\eta_1 > 0$, $\eta_2 > 0$ and $\alpha > 1$ which satisfies

$$\begin{aligned}
L &= A_1 L + A_2 I + A_3 C + \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2) \\
&\geq \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2) \sin ce A_i > 0, B_i > 0, i=1,2,3 \\
&\geq \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2) - B_1 \sin ce B_1 u_1^2 - B_1 \leq 0, \\
&\geq \min \left(\frac{1}{2} B_1, \frac{1}{2} B_2, \frac{1}{2} B_3 \right) (u_1^2 + u_2^2 + u_3^2) - B_1 \\
&\geq B \|u_1, u_2, u_3\|^2 - B_1, \text{ where } B = \min \left(\frac{1}{2} B_1, \frac{1}{2} B_2, \frac{1}{2} B_3 \right)
\end{aligned}$$

Hence, C5 is satisfied. We therefore conclude that there exists an optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ that minimizes the objective functional $J(u_1, u_2, u_3)$. $\square$

Characterization of the optimal controls

Here, we characterize the optimal controls (u_1^*, u_2^*, u_3^*) which give the optimal levels for the various control measures and the corresponding states $(S^*, L^*, I^*, C^*, R^*, V^*)$. The Pontryagin's Maximum Principle (PMP) [2] gives the necessary conditions that must be satisfied by an optimal control. PMP converts Equations (9) and (10) into a problem of point wise minimization of a Hamiltonian, H with respect to u_1, u_2 and u_3 . The Hamiltonian, H is defined as

$$H = L(S(t), L(t), I(t), C(t), R(t), V(t)) + \sum_{i=1}^3 \lambda_i^T g_i \quad (19)$$

where λ_i^j 's ($i = \{S, L, I, C, R, V\}$) are the co-state or adjoint variables.

Applying PMP [2] leads to the following result.

Theorem 2. Given an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in U$ and the solution $S^*, L^*, I^*, C^*, R^*, V^*$ associated to the state system, Model (18), then there exist adjoint variables $(\lambda_S, \lambda_L, \lambda_I, \lambda_C, \lambda_R, \lambda_V)$ satisfying

$$\begin{aligned}
\frac{d\lambda_S}{dt} &= (\lambda_S - \lambda_L)(1 - u_1)\beta(I + C) + (\lambda_S - \lambda_R)u_2 + \mu\lambda_S \\
\frac{d\lambda_L}{dt} &= -A_1 + (\lambda_L - \lambda_I)\alpha + \mu\lambda_L \\
\frac{d\lambda_I}{dt} &= -A_2 + (\lambda_S - \lambda_L)(1 - u_1)\beta S + (\lambda_I - \lambda_R)(\gamma + u_3) + (\lambda_R - \lambda_C) + \mu\lambda_I \\
\frac{d\lambda_C}{dt} &= -A_3 + (\lambda_S - \lambda_C)b\sigma(1 - \omega) + (\lambda_S - \lambda_L)(1 - u_1)\beta S + (\lambda_C - \lambda_R)(\delta + \phi + u_3) + \mu\lambda_C \\
\frac{d\lambda_R}{dt} &= (\lambda_R - \lambda_S)\varphi + \mu\lambda_R \\
\frac{d\lambda_V}{dt} &= (\lambda_R - \lambda_V)\psi + \mu\lambda_V
\end{aligned} \quad (20)$$

and the transversality conditions

together with the optimal controls given by

$$\lambda_i(T) = 0, \text{ for } i = \{S, L, I, C, R, V\} \quad (21)$$

$$\begin{aligned}
u_1^* &= \min \left\{ \max \left(0, \frac{(\lambda_L - \lambda_S) \beta S^* (I^* + C^*)}{B_1} \right), 1 \right\} \\
u_2^* &= \min \left\{ \max \left(0, \frac{(\lambda_S - \lambda_T) S^*}{B_2} \right), 1 \right\} \\
u_3^* &= \min \left\{ \max \left(0, \frac{(\lambda_I - \lambda_R) I^* + (\lambda_C - \lambda_R) C^*}{B_3} \right), 1 \right\}
\end{aligned} \tag{22}$$

Proof. Given the Hamiltonian:

$$\begin{aligned}
H &= A_1 L + A_2 I + A_3 C + \frac{1}{2} B_1 u_1^2 + \frac{1}{2} B_2 u_2^2 + \frac{1}{2} B_3 u_3^2 \\
&+ \lambda_S [b(1-\omega)(1-\sigma C) + \phi R - (1-u_1)\beta(I+C)S - (\mu + u_2)S] \\
&+ \lambda_T [(1-u_1)\beta(I+C)S - (\mu + \alpha)I] \\
&+ \lambda_L [\alpha L - (\mu + \gamma + u_3)I] \\
&+ \lambda_C [b\sigma(1-\omega)C + \rho\gamma I - (\mu + \delta + \phi + u_3)C] \\
&+ \lambda_R [(1-\rho)\gamma I + (\delta + \phi)C - (\mu + \phi)R - \psi V + u_3(I+C)] \\
&+ \lambda_V [b\omega + u_2 S + \psi V - \mu V].
\end{aligned} \tag{23}$$

Using PMP, Equation (19) is obtained from

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial i}, \text{ where } i = \{S, L, I, C, R, V\} \tag{24}$$

At the terminal time, T , all the state variables are free. Thus, transversality conditions have the form (20).

Maximizing H with respect to u_1, u_2, u_3 at $u^* = (u_1^*, u_2^*, u_3^*)$ leads to the differentiation of H with respect to u_1, u_2 and u_3 , respectively, which gives

$$\begin{aligned}
\frac{\partial H}{\partial u_1} &= B_1 u_1 - (\lambda_L - \lambda_S) \beta S (I + C) = 0 \text{ at } u_1 = u_1^* \\
\frac{\partial H}{\partial u_2} &= B_2 u_2 - (\lambda_S - \lambda_T) S = 0 \text{ at } u_2 = u_2^* \\
\frac{\partial H}{\partial u_3} &= B_3 u_3 - (\lambda_I - \lambda_R) I - (\lambda_C - \lambda_R) C = 0 \text{ at } u_3 = u_3^*
\end{aligned} \tag{25}$$

Solving for u_1^*, u_2^* and u_3^* on the interior of control set gives

$$\begin{aligned}
u_1^* &= \frac{(\lambda_L - \lambda_S) \beta S^* (I^* + C^*)}{B_1} \\
u_2^* &= \frac{(\lambda_S - \lambda_T) S^*}{B_2}
\end{aligned} \tag{26}$$

Upon imposing $u_3^* = \frac{(\lambda_I - \lambda_R) I^* - (\lambda_C - \lambda_R) C^*}{B_3}$

$$\begin{aligned}
u_1^* &= \min \left\{ \max \left(0, \frac{(\lambda_L - \lambda_S)\beta S^*(I^* + C^*)}{B_1} \right), 1 \right\} \\
u_2^* &= \min \left\{ \max \left(0, \frac{(\lambda_S - \lambda_I)S^*}{B_2} \right), 1 \right\} \\
u_3^* &= \min \left\{ \max \left(0, \frac{(\lambda_I - \lambda_R)I^* + (\lambda_C - \lambda_R)C^*}{B_3} \right), 1 \right\}
\end{aligned} \tag{27}$$

Using Equation (10) in equation Model (9), we obtain the optimality system given as

$$\begin{aligned}
\frac{dS^*}{dt} &= b(1-\omega)(1-\sigma C^*) + \varphi R^* - (1-u_1^*)\beta(I^* + C^*)S^* - (\mu + u_2^*)S^* \\
\frac{dL^*}{dt} &= (1-u_1^*)\beta(I^* + C^*)S^* - (\mu + \alpha)L^* \\
\frac{dI^*}{dt} &= \alpha L^* - (\mu + \gamma + u_3^*)I^* \\
\frac{dC^*}{dt} &= b(1-\omega)(1-\sigma)C^* + \rho I^* - (\mu + \delta + \phi + u_3^*)C^* \\
\frac{dR^*}{dt} &= (1-\rho)I^* + (\delta + \phi)C^* - (\mu + \varphi)R^* - \psi V^* + u_3^*(I^* + C^*) \\
\frac{dV^*}{dt} &= b\omega + u_2^*S^* + \psi V^* - \mu V^*
\end{aligned}$$

Numerical solution of the optimality system, Equations (19), (20), (21) and (27), is taken up in the next section.

Numerical Results and Discussion

For the numerical solutions, we carried out our simulations using MATLAB. We solve the optimality system, Equations (19), (20), (21) and (27), numerically using the fourth-order Runge-Kutta method. This method solves the state equations by choosing an initial guess for the controls u_1 , u_2 and u_3 forward in time. Afterward, the method solves the adjoint equations backward in time and then the controls are updated using Equation (26). For details on the forward-backward-sweep procedure, interested reader is referred to [8].

The values for initial conditions are obtained from [2,8]. We assumed values, which are biologically feasible, for φ and ψ , their values and the values for the remaining parameters are as presented in Table 3. In addition, we take the weight constants to be $A_i = 10$ (for $i = 1, 2, 3$.) and $B_i = 0.01$ (for $i = 1, 2, 3$.) The results obtained are presented by Figures 1-9.

Table(3): Parameter values used for the numerical simulation and their sources

Parameter	Value	Source
b	0.0121	[20]
ω	0.8	[19]
σ	0.11	[20]
ϕ	0.01	[20]
β	0.78	[Assumed]
μ	0.069	[20]
α	0.0012	[20]
γ	0.0208	[18]
ρ	0.6	[20]
δ	0.025	[28]
φ	0.01	[Assumed]
ψ	0.8	[Assumed]

Figures 1-6 present the transmission dynamic of susceptible, latent, acute, carrier, recovered and vaccinated individuals, respectively. Our goal of introducing optimal control strategy is to minimize the number of latent, acute and carrier individuals while maximizing the number of susceptible, recovered and vaccinated individuals. From Figure 3 and 4, it is observed that the population of acute and carrier individuals reduced to near zero during the fourth year of control intervention and remained there throughout the remaining period of intervention. Similarly, a significant reduction in the number of latent individuals in the presence of control interventions is noticeable in Figure 2. However, The number of recovered and vaccinated individuals increased throughout the years of control intervention as shown in Figures 5 and 6, respectively while the number of susceptible individuals started increasing as from the fourth year of control intervention as depicted in Figure 1.

Also, Figures 7, 8 and 9 represent the dynamic of the time-dependent control variables which account for isolation, vaccination and treatment, respectively. Figure 7 shows that the control isolation, u_1 reduces from its peak value of 25% to zero during the first four years and no consideration is given to it thereafter. The control vaccination, u_2 is set at upper bound during the first 2 months and decreases to zero during and after the second year of control intervention as shown in Figure 8. Similarly, Figure 9 shows that the control treatment (u_3) is set at the upper bound during the first 58 months of the intervention and decreases to the lower bound at the end of control intervention.

Figure(1): The susceptible population with and without control

Figure(2): The latent population with and without control

Figure(3): The acute population with and without control

Figure(4): The carrier population with and without control

Figure(5): The recovered population with and without control

Figure(6): The vaccinated population with and without control

Figure(7): The dynamic of control variable u_1 representing isolation

Figure(8): The dynamic of control variable u_2 representing vaccination

Figure(9): The dynamic of control variable u_3 representing treatment

Conclusion

This work presents both theoretical and quantitative analyses of a deterministic epidemiological model of a Gonorrhea disease infection. The results obtained are highlighted as follows:

1. The model is epidemiologically well posed
2. The solution exists and unique.

3. The disease-free equilibrium is locally asymptotically stable when the threshold quantity, R_0 , is less than one.
4. Increasing the value of any of the parameters with positive will increases the basic reproduction number, R_0 , and the magnitude of the infectious individual in the community increases accordingly. Conversely, increasing the value of the parameter decreases the basic reproduction number, R_0 , and the magnitude of the infectious individuals in the community decreases accordingly.
5. Three time-varying control variables are considered and a control strategy for the minimization of infected individuals with latent, infectious and chronic HBV was developed.

In summary, three time-varying control variables are considered and a control strategy for the minimization of infected individuals with latent, infectious and chronic HBV was developed. An Hepatitis B Virus (HBV) disease transmission with constant recruitment. The threshold parameter $R_0 < 1$, known as the Basic Reproduction Number was found. This model has two equilibria, disease-free equilibrium and endemic equilibrium. The Sensitivity analysis of the model was done.

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