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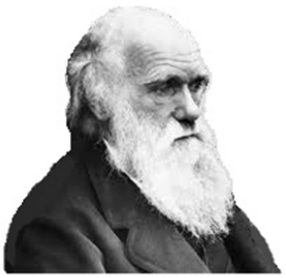

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Optimal Control Model for Hepatitis B Virus

Martins Onyekwelu Onuorah[1,*], Abdulahi Mohammed Baba[1], Nanangwe Alaisa[2], Robert Ssali Balagadde[3], Inncent Kabandana[4]

[1]Department of Mathematics & Statistics, School of Mathematics and Computing, Kampala International University, Main Campus, Kampala, Uganda

[2]Department of Education Science, Faculty of Education Open and Distance E-Learning, Kampala International University, Main Campus, Kampala, Uganda

[3]Department of Computer Science, School of Mathematics and Computing, Kampala International University, Main Campus, Kampala, Uganda

[4]Department of Computer Science, College of Science and Technology (CST), School of ICT, University of Rwanda, Kigali, Rwanda

*E-mail address: martins.onuorah@kiu.ac.ug

ABSTRACT

In this paper, we proposed an ordinary differential equation model for the transmission of Hepatitis B virus (BHV). The model accounted for the susceptible, exposed, infected, Chronic, and removed classes. We obtained the model's disease-free and endemic equilibrium points and the effective reproductive number. Further, from a thorough sensitivity analysis of the effective reproductive number, we extended the model by incorporating five time-dependent controls to cater to the vertical transmission, vaccination, testing, and treatment of acutely and chronically infected individuals. Numerical simulation was conducted to underscore the effects of the control in combating HBV.

***Keywords*:** Hepatitis, differential equation, optimal control, Pointwise hamiltonian, Lebesques measurable, equilibrium, stability, simulation, Hepatitis B virus, *Hepadnaviridea*

1. INTRODUCTION

Hepatitis B virus (HBV) is a DNA virus of the *Hepadnaviridea* family recognized globally as a significant disease of public health importance. It has been estimated that up to 2

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billion individuals have evidence of exposure, and 248 million persons are chronically infected. (Kiire, 1993). Epidemiologically, approximately 15–40% of chronically infected patients develop serious complications such as cirrhosis, liver failure, and hepatocellular carcinoma (HCC). Nearly 1 million people die annually as a result of these complications. (Nicolini et al., 2019). Most infected individuals are of eastern Asian or sub-Saharan African origin. Sub-Saharan Africa is considered to be a region of high endemicity with an average carrier rate of 10–20% in the general population and with 70–95% having at least a marker of previous infection (Emechebe et al., 2009; Schweitzer et al., 2015)

Several mathematical models have been proposed by researchers to understand the dynamics of HBV. Others have also used mathematical models to evaluate how control strategies have fared in combating HBV. These models are in the form of an ordinary differential equation, fractional order differential equation, stochastic differential equations, and integro-differential equations.

(Khatun & Biswas, 2020) presented a compartmental model of chronic disease liver cirrhosis describing the transmission dynamics of Hepatitis B. Their research aimed to minimize infected and liver cirrhotic individuals by applying two optimal control strategies of vaccination and treatment. Analytical and numerical analysis of their model shows that the two strategies can successfully combat the Hepatitis B virus. (Aniji et al., 2020) developed and analyzed a model to understand the effect of antiviral therapy using LHAM, which describes the possible relation to HBV and target liver cells. The paper analyzed how the number of infected cells largely gets reduced and how liver damage can be controlled. (Alrabaiah et al., 2020) presented the analysis of the Hepatitis B virus through a new mathematical model in the presence of treatment and vaccinations.

They extended the model to an optimal control problem of three control variables. Considering different control combinations, we introduce four different strategies to minimize the spread of Hepatitis B infection in the population. Finally, to illustrate the effectiveness of each strategy for the eradication of the disease, They perform and discuss the numerical simulations in detail. (Means et al., 2020) studied the role of spatial effects in mathematical models for the Hepatitis b virus. They summarised that animal models and in vitro experiments for HBV do not provide the level of delicate control over such spatial aspects provided by mathematical models. Construction of such a detailed, critical, tractable model may prove instrumental in detailing precisely why nearly 300 million people are persistently infected with HBV.

In (Volinsky et al., 2021) the authors present an analysis of a hepatitis B virus (HBV) model, including cytotoxic T lymphocytes (CTL) and antibody responses, under distributed feedback control, expressed as an integral form to predict the effect of a combination treatment with interleukin-2 (IL-2). They used Cauchy matrices to analyze the stability of the corresponding integrodifferential systems. (Side et al., 2021) built a Susceptible-Exposed-Infected-Recovered-Infected (SEIRI) model for HBV using the mathematical Graph method. (Zada et al., 2021) extended a constant control model to a suitable optimal control problem to reduce the number of humans that are infected with the Hepatitis B virus and the costs associated with the controls.

The results of the numerical simulations of the extended model show that the optimal combination of education campaign (awareness), treatment, and vaccination is the most efficient way to control the hepatitis B virus (HBV) infection. (Din et al., 2021) proposed various stages of the hepatitis B virus (HBV) besides its transmissibility and nonlinear

incidence rate to develop an epidemic model. Using sensitivity analysis, the authors formulate a control problem to eradicate HBV from the population and prove that the control problem exists. The optimum system's complete characterization was achieved using the 4th-order Runge-Kutta procedure.

(Volinsky, 2022) classified the equilibrium points of an HBV mathematical model with combined therapy. The influence of right-hand side changes on solution behaviours is estimated, and regulation with delays in upper- and lower-bound integral limits that presents a period with IL-2 support therapy are researched. (Din & Abidin, 2022) constructed a system of equations for Hepatitis B disease in the sense of Atanganaa– Baleanu Caputo (ABC) fractional order derivative. They used some well-known results of fixed point theory to find the Ulam–Hyers type stability. Further, they apply well-known transform due to Laplace and decomposition techniques (LADM) and Adomian polynomial for nonlinear terms to compute the proposed model's series solution. Graphical results show that LADM is an efficient and robust method for solving nonlinear problems. (Fatehi et al., 2022) presented an age-structured model for the immune response to an HBV infection, considering contributions from cell-mediated and humoral immunity. The impacts of immune response exhaustion and non-infectious subviral particles on the immune response dynamics were analyzed. A comparison of different treatment options in the context of this model reveals that drugs targeting aspects of the viral life cycle are more effective than exhaustion therapy, a form of therapy mitigating immune response exhaustion. Their model was validated using published patient data recorded during acute infection.

(Din & Li, 2022) presented a detailed analysis of a stochastic delayed model which governs the transmission mechanism of the Hepatitis B virus (HBV) while considering the white noises and the effect of vaccinations. The model was extended to a stochastic model. By utilizing the concepts of stochastic theory and by constructing appropriate Lyapunov functions, they developed the theory for the extinction and persistence of the disease. Further, their model was shown to be ergodic and has a unique stationary distribution. The stochastic bifurcation theory was utilized, and a detailed bifurcation analysis of the model is presented. Using the standard curve fitting tools, they fitted the model against the available HBV data in Pakistan from March 2018 to February 2019 and accordingly, the model parameters were estimated. (Manna & Hattaf, 2022) In this paper, we formulate a generalized hepatitis B virus (HBV) infection model with two modes of infection transmission and adaptive immunity and investigate its dynamical properties. Five equilibria of the model are identified in terms of five threshold parameters (Formula presented.), and (Formula presented.). Further, the global stability analysis of each equilibrium under certain conditions was carried out by employing the suitable Lyapunov function and LaSalle's invariance principle. Finally, they presented an example with numerical simulations to illustrate the applicability of our study. Nonetheless, the results obtained in this study are valid for a wide class of HBV infection models.

(Elkhadir et al., 2022) formulated a mathematical model of the hepatitis B virus with vaccination and treatments as control strategies. The Stability analysis of the model was discussed, and the disease-free equilibrium and endemic equilibrium points were obtained. Sensitivity analysis for the parameters that could reduce the spread of the hepatitis B virus was studied. Finally, the numerical simulation shows that increasing the value of the vaccine in the immunized compartment or in the suspected compartment may decrease the value of R0, reducing the spread of the disease. (Dano et al., 2022) proposed and analyzed the combined effect of hepatitis B virus (HBV) infection and heavy alcohol consumption on the progression

dynamics of liver cirrhosis. To study the progression dynamics of cirrhosis and to describe the effect of alcohol intake variation on a chronic hepatitis B patient a deterministic model and a logistic function are considered, respectively. They established and proved the existence of theorems for forward and backward bifurcations. Finally, numerical simulations reveal that heavy alcohol consumption significantly accelerates the progression of liver cirrhosis in chronic hepatitis B-infected individuals. (Asfaw Wodajo & Tibebu Mekonnen, 2022) offered HBV virus transmission characteristics in the form of a mathematical model with immigration, vaccination, and HBV reactivation after recovery, as well as control measures for Hepatitis B virus disease transmission. The study's findings show that vaccination and treatment interventions play a critical role in reducing HBV transmission and reproduction. It was also demonstrated that HBV reactivation contributes significantly to an increase in the infective population, which boosts virus transmission, and that a combination of vaccination and treatment will be the most effective strategy for controlling HBV infection and reinfection after recovery.

(Aziz ur Rehman et al., 2023) studied the numerical solution of nonlinear delayed Immunized Susceptible Latent Infected and Recovered (MSLIR) epidemic model of HBV disease. They Euler, RK-4 and the non-standard finite difference (NSFD) techniques for the numerical solution of the model. The proposed (NSFD) technique becomes a more efficient and reliable numerical technique than the forward Euler and RK-4 scheme. (Yavuz et al., 2023) used the Adams–Bashforth numerical scheme to study the behaviours of the Hepatitis-B virus (Hepatitis-B). They applied the parameter estimation method to determine model parameters and find the curve that best fits the model. The stability analysis of the model was considered, and the sensitivity analysis of R0 is examined. The results point out that the order of the fractional derivative has an essential effect on the dynamical process of the constructed model for Hepatitis-B.

(Ma & Ma, 2023) investigated the dynamics of a stochastic HBV transmission model with media coverage and saturated incidence rate. They obtained the conditions on the extinction of HBV, which implies that media coverage helps to control the disease spread and the noise intensities on the acute and chronic HBV infection play a key role in disease eradication. As a case study, their model fitted to the available hepatitis B data of mainland China from 2005 to 2021. (Schmit et al., 2023) used a mathematical model of HBV transmission and natural his- tory, calibrated to all available West African data, to project the population-level health impact and cost-effectiveness of different monitoring strategies for HBV-infected individuals not initially eligible for antiviral treatment. They concluded that monitoring less frequently than once a year is a cost-effective strategy in a community-based HBV screening and treatment program in The Gambia. The optimal strategy depends on the cost-effectiveness threshold. In this paper, we proposed an ordinary differential model for the transmission dynamics of Hepatitis B virus (HBV); our model included the susceptible, exposed, infected, Chronic, and removed individuals. We will incorporate vertical transmission and vaccination and extend the model to the optimal control problem.

2. MODEL FORMULATION

Our model consists of the human population at time t represented by $N(t)$, which is further divided into five mutually exclusive compartments representing the susceptible human

who are at risk of contracting HBV $S(t)$, newly infected individuals who contracted HBV which is at the incubation stage $E(t)$, acute infected individuals whose infection has being diagnosed and are at the infectious stage $I(t)$, the chronic infected individuals $C(t)$, who whose infections where not diagnosed on time or whose infection has persisted for a long time, the individuals are at high risk of liver cirrhosis. Finally, we have the removed compartment $R(t)$, for the individuals who received the HBV vaccine and those who recovered from acute of chronic infections.

Thus, our model is represented as in (1) with parameter values given in Table 1.

$$\begin{aligned}
\frac{dS}{dt} &= (1-\tau)\psi + (1-\upsilon)\psi - (\alpha_1 C + \alpha_2 I)S - \mu S,\\
\frac{dE}{dt} &= (\alpha_1 C + \alpha_2 I)S - (\sigma_1 + \sigma_2 + \mu)E,\\
\frac{dI}{dt} &= \tau\psi + \sigma_1 E - (\mu + \delta_1 + \gamma_1)I,\\
\frac{dC}{dt} &= \sigma_2 E - (\mu + \delta_2 + \gamma_2)C,\\
\frac{dR}{dt} &= \upsilon\psi + \gamma_1 I + \gamma_2 C - \mu R.
\end{aligned} \tag{1}$$

Such that $N(t) = S(t) + E(t) + I(t) + C(t) + R(t)$ representing the entire human population.

Table 1. Model Parameters and their values

Parameter, their meaning, and values			
τ	Vertical transmission rate	0.071	Assumed
ψ	Birth rate of human	0.0012	Estimated
υ	Vaccination against HBV	0.86	Estimated
α_1	The transmission rate of acutely infected humans	0.00034	Assumed
α_2	The transmission rate of Chronically infected humans	0.00005	Assumed
μ	The natural death rate of humans	0.02	Estimated
σ_1	Rate of progression from exposed to acute infection	10.3	Assumed
σ_2	Rate of progression from exposed to chronic infection	6.5	Assumed
γ_1	The recovery rate of acute infection	0.5	Estimated

γ_2	The recovery rate of chronic infection	0.3	Estimated
δ_1	The death rate due to acute infection	0.01	Assumed
δ_2	The death rate due to chronic infection	0.05	Assumed

2. 1. Basic Properties

In this section, we explore the basic dynamical features of the model (1). We make the following claims:

Lemma 1

$D = \left\{(S,E,I,C,R) \in R_+^5 : S+E+I+C+R \le \frac{\psi(\tau+\upsilon-2)}{\mu}\right\}$, is positively invariant and attracting with respect to the basic model equations (1).

Proof

Adding equations four equations of (1) gives:

$$\frac{dN}{dt} = \psi - \delta_1 I + \delta_2 C - \mu N. \qquad (2)$$

Since $\frac{dN}{dt} < \psi - \mu N$, it follows that $\frac{dN}{dt} < 0$ if, $N(t) > \frac{\psi}{\mu}$.

Thus, by the standard comparison theorem, we show that,

$N(t) < N(0)e^{-\mu(t)} + \frac{\psi}{\mu}\left[1-e^{-\mu(t)}\right]$. In particular, $N(t) \le \frac{\psi}{\mu}$. Thus, D is positively invariant. Further, if $N(t) > \frac{\psi}{\mu}$, then either the solution enters D in finite time or $N(t)$ approaches $\frac{\psi}{\mu}$, and the infected variables E, I, C approaches zero. Hence, all solutions R_+^5 eventually enters D. Thus in D, the basic model (1) is well posed epidemiologically and mathematically (Searles et al., 2017) and (Hethcote, 2000). Hence, it is sufficient to study the dynamics of the model equations in D.

Lemma 2

Let the initial data $F(0) \ge 0$, where $F(t) = (S,E,I,C,R.$ Then the solution $F(t)$ of the model (1) are non- negative for all $t \ge 0$. Furthermore form (1) and (2),

$$\lim_{t\to\infty} \sup N(t) = \frac{\psi}{\mu}.$$

Proof

$t_1 = \sup\{t > 0 : F(t) > 0 \in [0,t]\}$. Thus $t_1 > 0$. It follows from the first equation of (1):

$\frac{dS}{dt} = (1-\tau)\psi + (1-\upsilon)\psi - (\alpha_1 C + \alpha_2 I)S - \mu S$, which can also be written as:

$$\frac{d}{dt}\left\{S(t)\exp\left[\alpha_1\int_0^{t_1} I(\xi)d\xi + \alpha_2\int_0^{t_1} Cd\xi + (\mu)t\right]\right\}$$

$$= (1-\tau)\psi + (1-\upsilon)\psi\exp\left[\alpha_1\int_0^{t_1} I(\xi)d\xi + \alpha_2\int_0^{t_1} Cd\xi + (\mu)t\right].$$

So that,

$$\frac{dS(t_1)}{dt}\exp\left[\alpha_1\int_0^{t_1} I(\xi)d\xi + \alpha_2\int_0^{t_1} Cd\xi + (\mu)t + (\mu)t\right] - S(0)$$

$$= (1-\tau)\psi + (1-\upsilon)\psi\exp\left[\alpha_1\int_0^{P} I(\xi)d\xi + \alpha_2\int_0^{P} Cd\xi + (\mu)p\right]dp.$$

Hence,

$$S(t_1) = S_1(0)\exp\left[\alpha_1\int_0^{t_1} I(\xi)d\xi + \alpha_2\int_0^{t_1} Cd\xi + (\mu)t + (\mu)t\right]$$

$$+\exp\left[\alpha_1\int_0^{t_1} I(\xi)d\xi + \alpha_2\int_0^{t_1} Cd\xi + (\mu)t + (\mu)t\right]\cdot\int_0^{t_1}(1-\tau)\psi + (1-\upsilon)\psi\exp\left[\alpha_1\int_0^{P} I(\xi)d\xi + \alpha_2\int_0^{P} Cd\xi + (\mu)t\right]dp > 0.$$

Similarly, it can be shown that $F > 0$, for all $t > 0$. For the second part of the proof, note that:

$0 < E(t) \le N(t), 0 < I(t) \le N(t), 0 < C(t) \le N(t), 0 < R(t) \le N(t).$

From equations (1) and (2)

$\frac{\psi}{\mu} \le \underset{t\to\infty}{Lim}\inf N(t) \le \underset{t\to\infty}{Lim}\sup N(t) = \frac{\psi}{\mu}$, as required.

2. 2. Disease-free equilibrium (DFE)

At equilibrium points, the rate of change of the state variables is zero, that is:

$$\frac{dS(t)}{dt}=\frac{dE(t)}{dt}=\frac{dI(t)}{dt}=\frac{dC(t)}{dt}=\frac{dR(t)}{dt}=0 \tag{3}$$

Disease-free equilibrium is an equilibrium where there is no infection. Therefore, the infected classes will be zero, making the whole population susceptible. To find the disease-free equilibrium of our model equations (1), we equate the rate of change of the non-infectious states to zero and completely ignore the infectious classes as they will be zero.

$$E^{*}=(S^{*},E^{*},I^{*},C^{*},R^{*})=\left(\frac{\psi(\tau+\upsilon-2)}{\mu},0,0,0,\frac{\psi\upsilon}{\mu}\right). \tag{4}$$

2. 3. Endemic equilibrium

Endemic equilibrium is an equilibrium state where none of the state variables is zero. To obtain the endemic equilibrium of our model, we solve equation (1) simultaneously.

$$\begin{aligned}
S^{**}&=\frac{(\mu^2+\mu\delta_2+\mu\gamma_2+\mu\sigma_1+\mu\sigma_2+\delta_2\sigma_1+\delta_2\sigma_2+\gamma_2\sigma_1+\gamma_2\sigma_2}{\alpha_1\sigma_2},\\
E^{**}&=\frac{\left(\begin{array}{l}\psi\upsilon\alpha_1\sigma_2+\mu^3+\mu^2\delta_2+\mu^2\gamma_2+\mu^2\sigma_1+\mu^2\sigma_2+\mu\delta_2\sigma_1\\+\mu\delta_2\sigma_2+\mu\gamma_2\sigma_2+\mu\gamma_2\sigma_2-\psi\alpha_1\sigma_2+\tau\alpha_1\sigma_2-\alpha_1\sigma_2\end{array}\right)}{\sigma_2(\sigma_1+\sigma_2+\mu)\alpha_1},\\
I^{**}&=\frac{\left(\begin{array}{l}\psi\upsilon\alpha_1\sigma_2+\mu^3+\mu^2\delta_2+\mu^2\gamma_2+\mu^2\sigma_1+\mu^2\sigma_1\\+\mu\delta_2\sigma_1+\mu\gamma_2\sigma_1+\mu\gamma_2\sigma_1-\psi\alpha_1\sigma_1+\tau\alpha_1\sigma_2-\alpha_1\sigma_2\end{array}\right)}{\gamma_1(\mu^2+\mu\delta_2+\mu\gamma_2+\sigma_1\mu+\mu\sigma_2+\delta_2\sigma_1+\delta_2\sigma_2},\\
C^{**}&=\frac{\left(\begin{array}{l}\psi\upsilon\alpha_1\sigma_2+\mu^3+\mu^2\delta_2+\mu^2\gamma_2+\mu^2\sigma_1+\mu^2\sigma_2+\mu\delta_2\sigma_1\\+\mu\delta_2\sigma_2+\mu\gamma_2\sigma_2+\mu\gamma_2\sigma_2-\psi\alpha_1\sigma_2+\tau\alpha_1\sigma_2-\alpha_1\sigma_2\end{array}\right)}{\alpha_1(\mu^2+\mu\delta_2+\mu\gamma_2+\sigma_1\mu+\mu\sigma_2+\delta_2\sigma_1+\delta_2\sigma_2+\gamma_2\sigma_1+\gamma_2\sigma_2},\\
R^{**}&=\frac{\left(\begin{array}{l}\mu(\sigma_1+\sigma_2+\mu)\gamma_2^2\\+\left(\begin{array}{l}\mu^3+(\delta_2+\sigma_1+\sigma_2)\mu^2+(-\psi\tau\alpha_1+\\\delta_2(\sigma_1+\sigma_2))\mu-(((\tau-\upsilon+1)\psi-\tau+1)\sigma_2+\psi\tau\sigma_1)\alpha_1\end{array}\right)\gamma_2\\-\psi\tau\sigma_1(\sigma_1+\sigma_2+\mu)(\mu+\delta_2)\end{array}\right)}{\alpha_1(\sigma_1+\sigma_2+\mu)(\mu+\delta_2+\gamma_2)\mu}.
\end{aligned} \tag{5}$$

2. 4. The basic reproductive number

These models usually have a threshold parameter, known as the basic reproductive number R_0 such that when $R_0<1$, then the DFE is locally asymptotically stable, and the disease cannot invade the population, but if $R_0>1$, then the DFE is unstable and invasion is always possible see (Hethcotet, 2000). We use the next-generation matrix approach as described by (Driessche & Watmough, 2002) to derive our effective reproductive number, which is the number of secondary infections resulting from the introduction of a single infected individual into a population where a proportion is fairly protected.

Definitions

1. $f_i(x)$ Is the rate of appearance of a new infection in compartment i.
2. $V_i^+(x)$ Is the rate of transfer of individuals into compartment i by all other means.
3. $V_i^-(x)$ Is the rate of transfer of individual out of the compartment i.
4. $V_i = V_i^- - V_i^+$.

Here, the basic reproductive number R_0 is the spectral radius (dominant eigenvalue) of the product matrix FV^{-I}, i.e. $R_0 = \rho(FV^{-I})$.

Our model has three Infective compartments namely the exposed human E, infected human I, and chronically infected human C. It follows that the matrices F and V for the new infective terms and remaining transfer terms respectively are given below. Where the entries of F and V are partial derivatives of $f_i(x)$, and $v_i(x)$. For our model, F and V are given below.

$$F = \begin{pmatrix} 0 & -\alpha_2 S^* & -\alpha_1 S^* \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} -(\sigma_1 + \sigma_2 + \mu) & 0 & 0 \\ \sigma_1 & -(\mu + \delta_1 + \gamma_1) & 0 \\ \sigma_2 & 0 & -(\mu + \delta_2 + \gamma_2) \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \dfrac{\alpha_2\sigma_1 S^*}{(\sigma_1 + \sigma_2 + \mu)(\mu + \delta_1 + \gamma_1)} + \dfrac{\alpha_1\sigma_2 S^*}{(\sigma_1 + \sigma_2 + \mu)(\mu + \delta_2 + \gamma_2)} & \dfrac{\alpha_2 S^*}{(\mu + \delta_1 + \gamma_1)} & \dfrac{\alpha_2 S^*}{(\mu + \delta_2 + \gamma_2)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$R_c = \frac{\alpha_2\sigma_1 S^*(\mu + \delta_2 + \gamma_2) + \alpha_1\sigma_2 S^*(\mu + \delta_1 + \gamma_1)}{(\mu + \delta_1 + \gamma_1)(\mu + \delta_2 + \gamma_2)(\sigma_1 + \sigma_2 + \mu)}. \qquad (6)$$

2. 5. Sensitivity analysis of the effective reproductive number (R_c)

Here we present the sensitivity index of the parameters of the effective reproductive number (R_c). Sensitivity Analysis is commonly used to determine the robustness of model prediction to parameter values since there are usually errors in data collection and presumed parameter values. It is used to determine parameters that have a high impact on the (R_c), which should be targeted by intervention strategies. The sensitivity indices of the effective reproductive number Table 2 and their graphs (Figures 1 to 12) are presented below.

Table 2. Sensitivity index of the effective reproductive numer

Parameter	Sensitivity sign
α_1	+1.67
γ_2	-1.47
σ_1	-1.29
σ_2	+1.29
μ	-1.02
ψ	1.00
υ	-0.80
α_2	-0.673
γ_1	+0.624
τ	-0.060
δ_2	+0.002
δ_1	-0.001

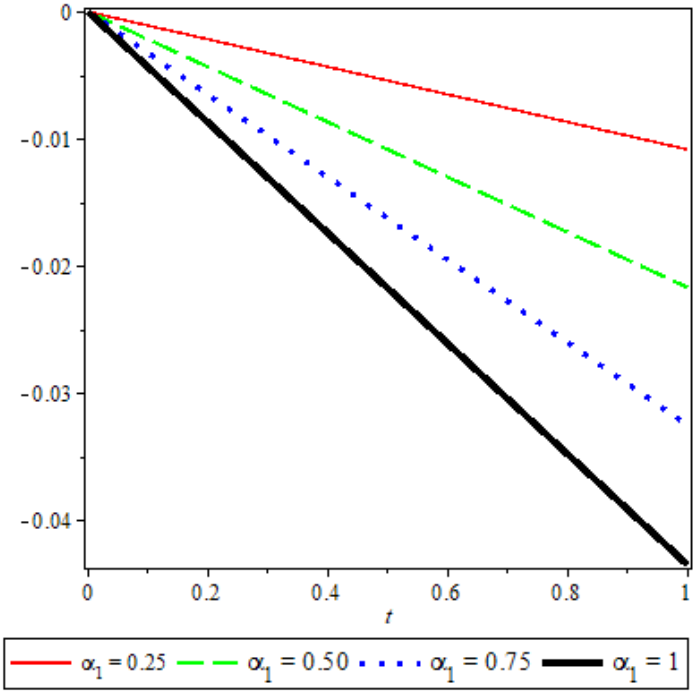

Figure 1. Shows the effect of the transmission rate of acute infected human. Which shows population reduction. It is the most sensitive parameter to the transmission of the disease

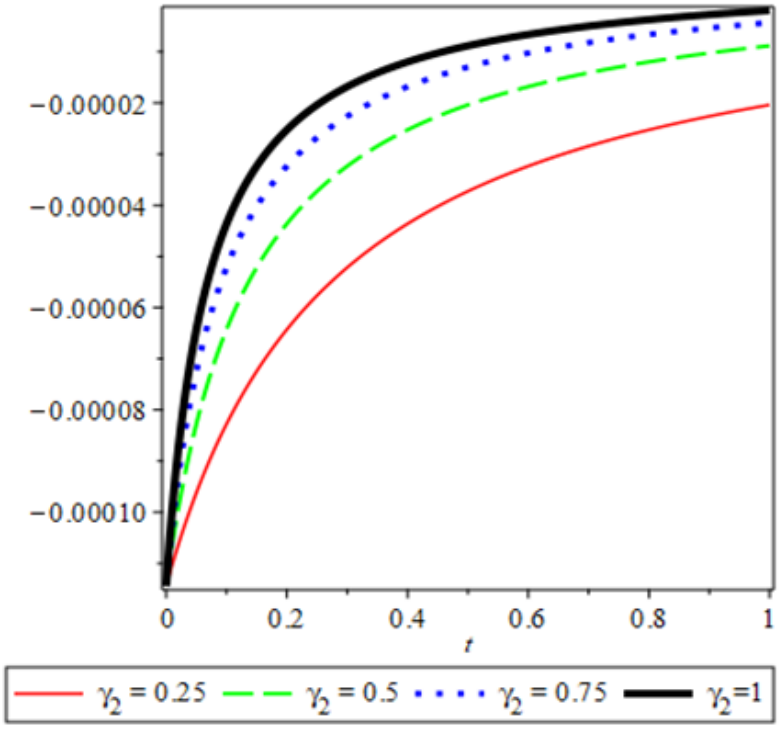

Figure 2. Shows the effect of the recovery rate of chronic infection, which is the next most sensitive parameter to the transmission of the disease

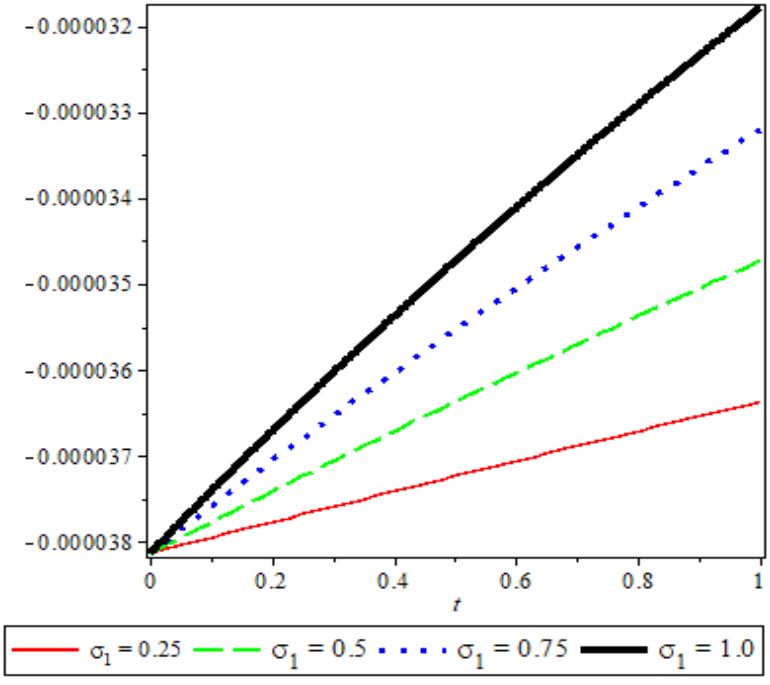

Figure 3. Shows the effect rate of progression from exposed to acute infection. It shows population reduction

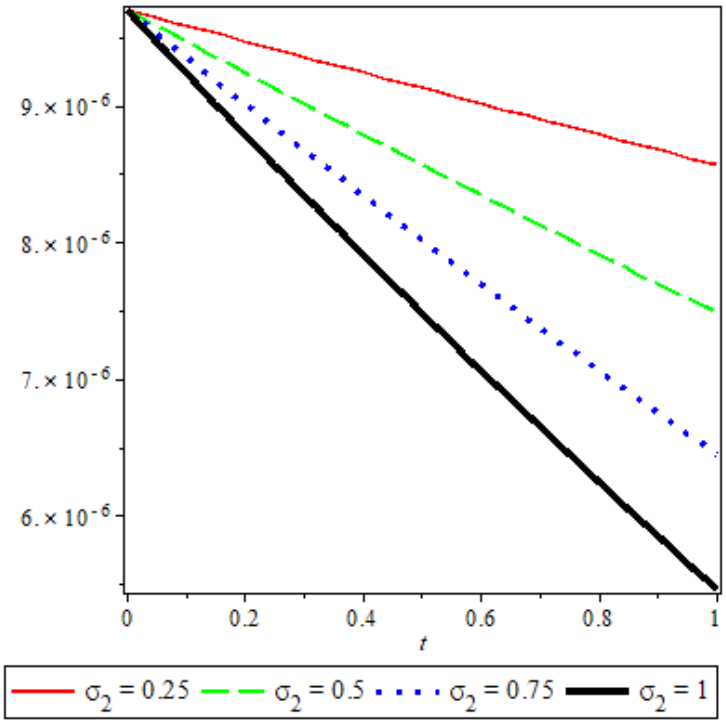

Figure 4. Shows the effect of the rate of progression from exposed to chronic infection. It shows population reduction

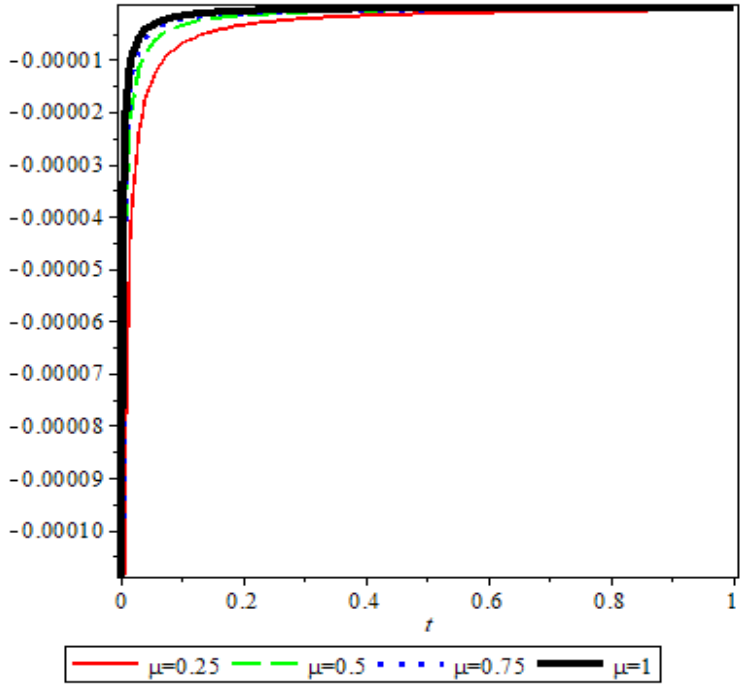

Figure 5. Shows the effect of the natural death rate of humans; it shows a decline in population

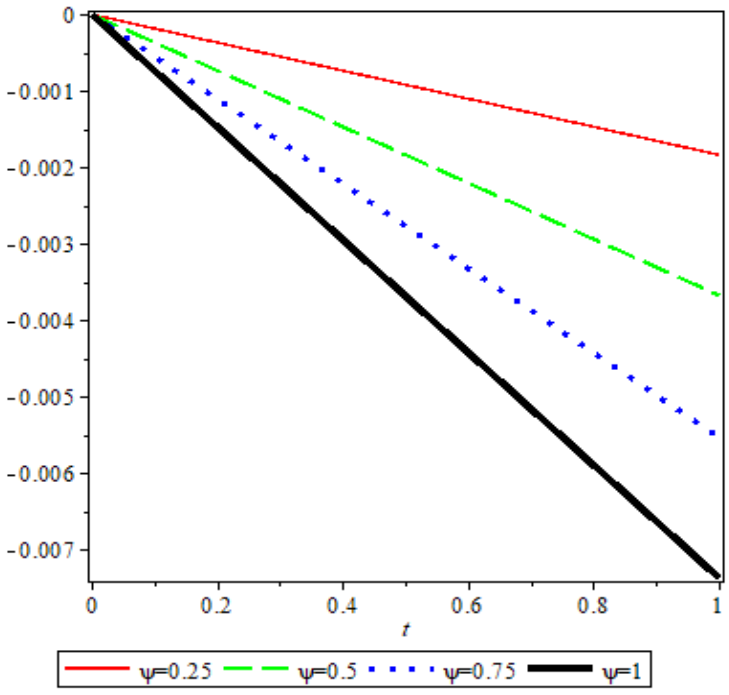

Figure 6. Shows the effect of the birth rate of humans on the disease transmission

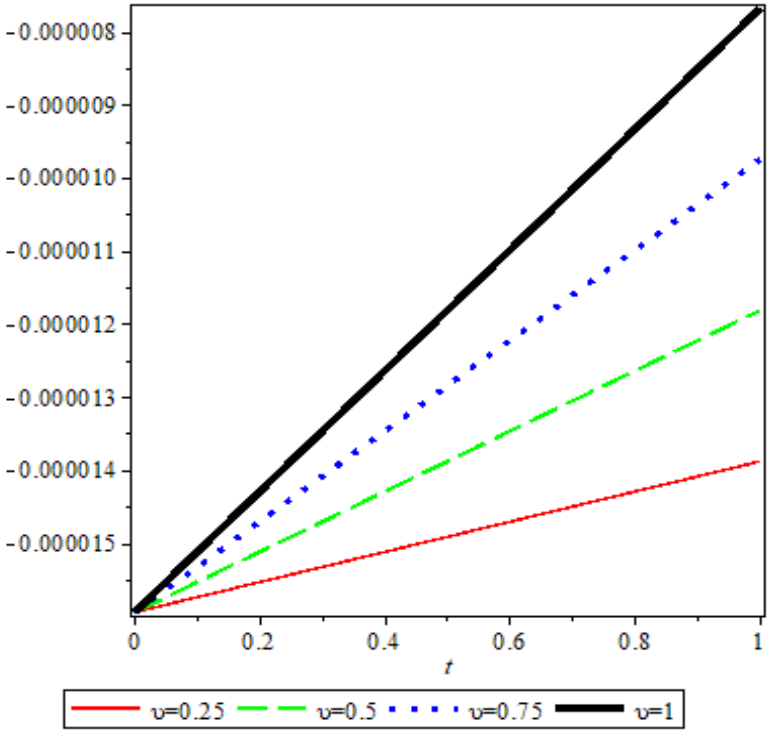

Figure 7. Shows the effect of Vaccination against HBV in disease transmission. The higher the percentage vaccinated, the higher the population growth

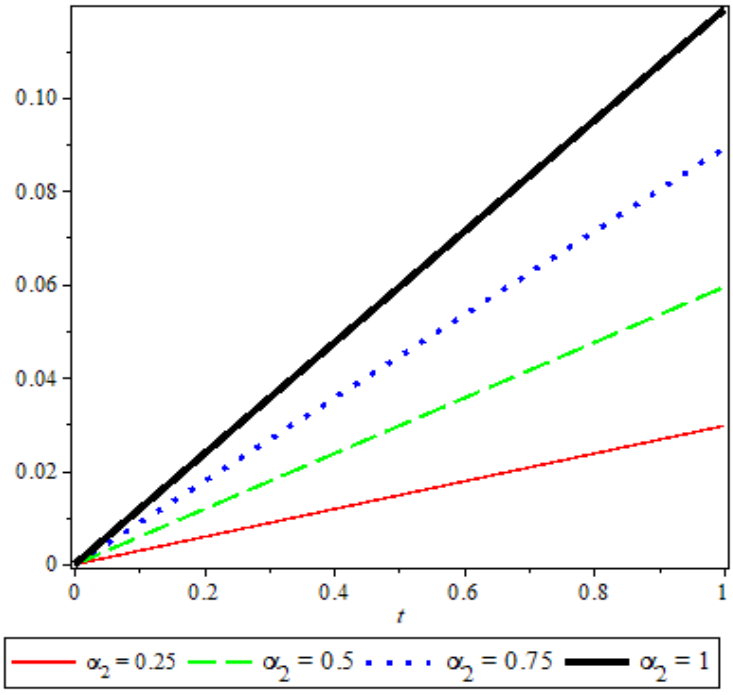

Figure 8. Shows the effect of the transmission rate of Chronically infected human. The higher the percentage of infectivity the higher the population of those infected.

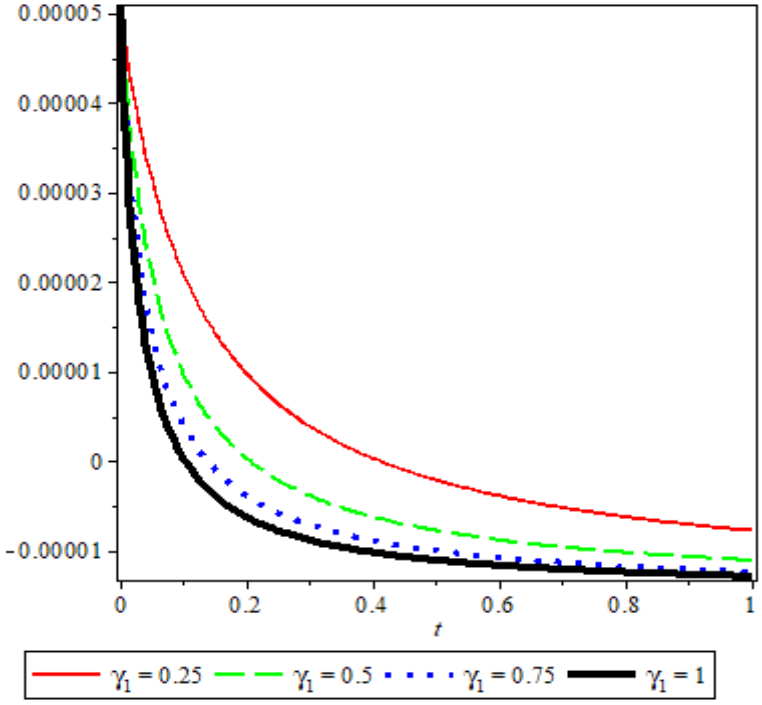

Figure 9. Shows the effect of recovery rate of acute infection. The higher the percentage of infectivity the higher the population of those infected

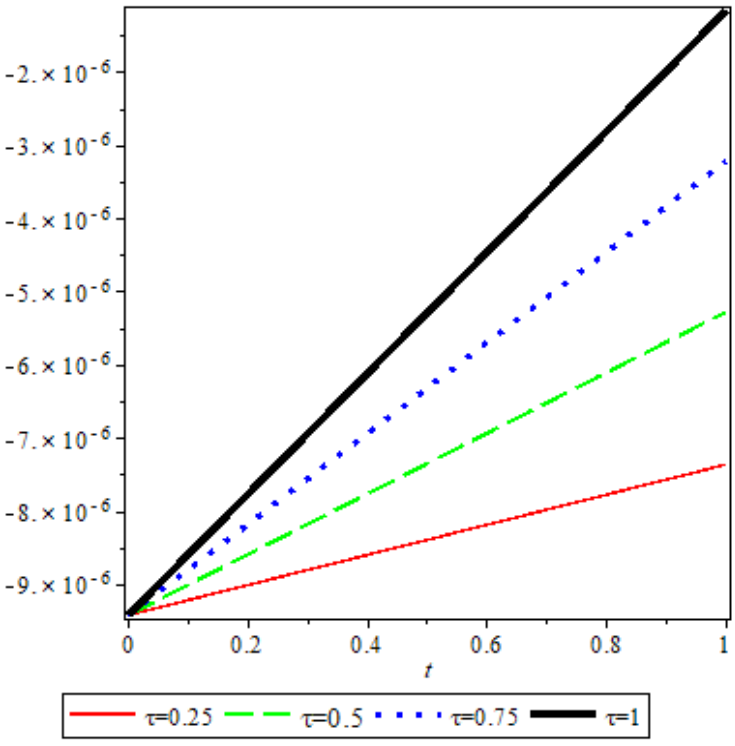

Figure 10. Shows the effect of Vertical transmission rate. The higher the percentage of Vertical transmission rate the higher the population of those infected

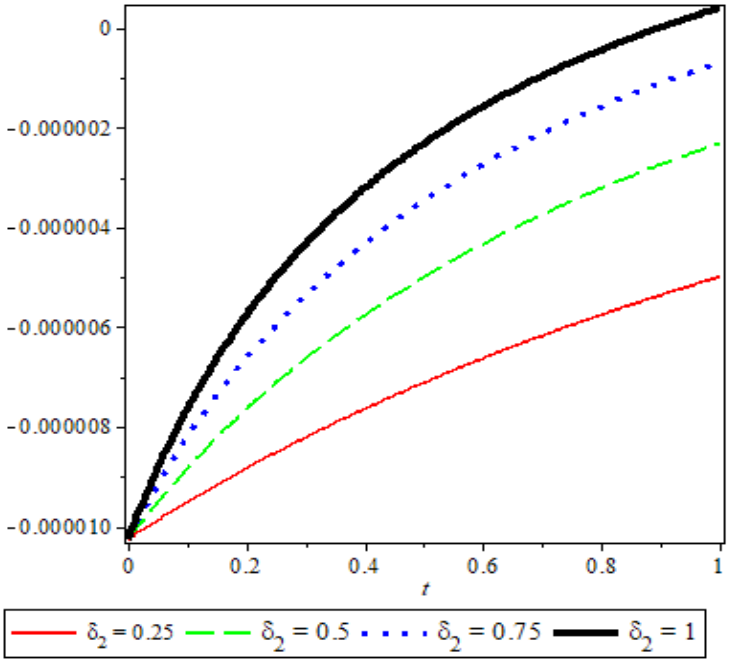

Figure 11. Shows the effect of death rate due to chronic infection. The higher the mortality, the less the population

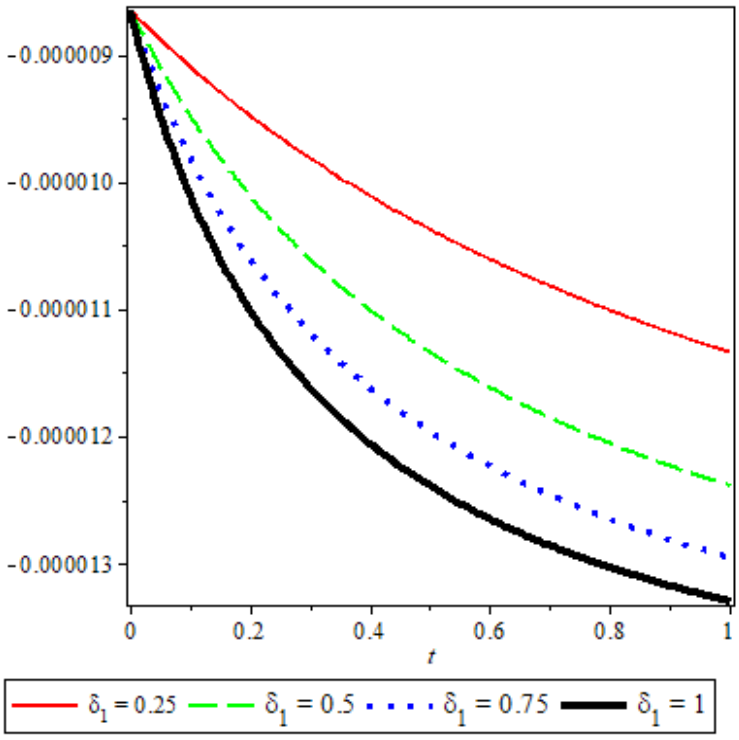

Figure 12. Shows the effect of death rate due to acute infection. The higher the mortality, the less the population

3. OPTIMAL CONTROL MODEL

$$\begin{aligned}
\frac{dS}{dt} &= (1-\tau)\psi + (1-u_1\upsilon)\psi - (1-u_2)(\alpha_1 C + \alpha_2 I)S - \mu S,\\
\frac{dE}{dt} &= (1-u_2)(\alpha_1 C + \alpha_2 I)S - (u_3(\sigma_1+\sigma_2)+\mu)E,\\
\frac{dI}{dt} &= \tau\psi + u_3\sigma_1 E - (\mu+\delta_1+u_4\gamma_1)I,\\
\frac{dC}{dt} &= u_3\sigma_2 E - (\mu+\delta_2+u_5\gamma_2)C,\\
\frac{dR}{dt} &= u_1\upsilon\psi + u_4\gamma_1 I + u_5\gamma_2 C - \mu R.
\end{aligned} \tag{7}$$

u_1 is the cost of vaccination against HBV, u_2 is the cost associated with prevention of infection via education and public enlightenment, u_3 is the cost associated with testing, this will determine if the HBV is acute or chronic, u_4 is the cost associated with the treatment of acute HBV, and u_5 is the cost associated with the treatment of chronic HBV. The separation of

treatment at acute and chronic levels is necessitated by the fact that at the chronic level, multiple organs may be affected; hence, more cost is expected.

The optimal control model above has associated objective function given by:

$$J(u) = \int_0^T \left(A_1 I + A_2 C + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2\right) dt \tag{8}$$

subject to the system (1).

where T the terminal time and the coefficients are $A_1, A_2, B_1, B_2, B_3, B_4, and\ B_5$ positive weights to balance the factors. The objective is to minimize the number of I and C while minimizing the cost coefficients $u_1(t), u_2(t), u_3(t), u_4(t),$ and $u_5(t)$. Thus, we seek an optimal control $u_1^*, u_2^*, u_{3,}^*\ u_4^*, u_{5,}^*$ such that where the control set is defined as;

$$u = \left\{u_1^*, u_2^*, u_3^*, u_4^*, u_5^* \middle| u_i(t)\ is\ Lebesques measurable, i = 1,2,3,4,5 0 \le u_i(t) \le 1, t \in [0,T]\right\}.$$

3. 1. Pontryagin's Invariant Principle

The Pontryagin's Invariant principle will be used to determine the necessary and sufficient conditions for our optimal control problem to hold. The principle will convert equations (1) and (8) to a minimization problem pointwise Hamiltonian (H) with respect to u_1, u_2, u_3, u_4, u_5..

$$\begin{aligned} H &= A_1 I_1 + A_2 I_2 + B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2 + B_4 u_4^2 + B_5 u_5^2 \\ &+ \lambda_1 \{(1-\tau)\psi + (1-u_1\upsilon)\psi - (1-u_2)(\alpha_1 C + \alpha_2 I)S - \mu S\} \\ &+ \lambda_2 \{(1-u_2)(\alpha_1 C + \alpha_2 I)S - (u_3(\sigma_1 + \sigma_2) + \mu)E\} \\ &+ \lambda_3 \{\tau\psi + u_3\sigma_1 E - (\mu + \delta_1 + u_4\gamma_1)I\} \\ &+ \lambda_4 \{u_3\sigma_2 E - (\mu + \delta_2 + u_5\gamma_2)C\} \\ &+ \lambda_5 \{u_1\upsilon\psi + u_4\gamma_1 I + u_5\gamma_2 C - \mu R\}. \end{aligned} \tag{9}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ are adjoint state variables.

Theorem 1

Given optimal controls $u_1(t), u_2(t),\ u_3(t)$, and solutions $S^*, E^*, I^*, C^*, R^*,$ of system (14) that optimizes $J(u_i)$ over u, then there exist adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5,$ satisfying $\frac{\partial \lambda_i}{\partial t} = -\frac{\partial H}{\partial_i}, \lambda_i(t) = 0, i = S^*, E^*, I^*, C^*, R^*.$

$$
\begin{aligned}
-\frac{d\lambda_1}{dt} &= \lambda_1(-(1-u_2)(\alpha_1 C+\alpha_2 I)-\mu)+\lambda_2(1-u_2)((\alpha_1 C+\alpha_2 I)),\\
-\frac{d\lambda_2}{dt} &= \lambda_2(-u_3(\sigma_1+o_2)-\mu)+\lambda_3 u_3\sigma_1+\lambda_4 u_3\sigma_2,\\
-\frac{d\lambda_3}{dt} &= A_1-\lambda_1(1-u_2)\alpha_2 S+\lambda_2(1-u_2)\alpha_2 S+\lambda_3(-u_4\gamma_1-\mu-\delta_1)+\lambda_5 u_4\gamma_1,\\
-\frac{d\lambda_4}{dt} &= A_2-\lambda_1(1-u_2)\alpha_1 S+\lambda_2(1-u_2)\alpha_1 S+(-u_5\gamma_2-\mu-\delta_2)\lambda_4+\gamma_2\lambda_5 u_5,\\
-\frac{d\lambda_5}{dt} &= -\lambda_5\mu.
\end{aligned}
\tag{10}
$$

and with transversality conditions $\lambda_1=\lambda_2=\lambda_3=\lambda_4=\lambda_5=0.$, and the control u^* satisfying the optimality conditions given by $\frac{\partial H}{\partial u_i}=0, i=1,2,3.$

$$
\left.
\begin{aligned}
u_1^* &= \max\left\{0,\min\left(1,-\frac{\psi\upsilon(-\lambda_1+\lambda_5)}{2B_1}\right)\right\},\\
u_2^* &= \max\left\{0,\min\left(1,\frac{S(-C\alpha_1\lambda_1+C\alpha_1\lambda_2-\alpha_2\lambda_1 I+\alpha_2\lambda_2 I)}{2B_2}\right)\right\},\\
u_3^* &= \max\left\{0,\min\left\{1,-\frac{E(-\lambda_2\sigma_1-\lambda_2\sigma_2+\sigma_1\lambda_3+\sigma_2\lambda_4}{2B_3}\right\}\right\},\\
u_4^* &= \max\left\{0,\min\left\{1,-\frac{I\gamma_1(\lambda_5-\lambda_3)}{2B_4}\right\}\right\},\\
u_5^* &= \max\left\{0,\min\left\{1,-\frac{C\gamma_1(\lambda_5-\lambda_4)}{2B_5}\right\}\right\}.
\end{aligned}
\right\}
\tag{11}
$$

Proof.

The optimal control problem exists provided that the integral of J with respect to the controls u_1, u_2, u_3 is convex and satisfies the Lipschitz conditions of the state variables. By equating the derivatives of the Hamiltonian with respect to the controls to zero (Abdullahi et al., 2015; Okosun et al., 2019; Osman et al., 2020), we have

$$\left.\begin{aligned} u_1 = \bar{u}_1 &:= \left(-\frac{\psi\upsilon(-\lambda_1 + \lambda_5)}{2B_1} \right), \\ u_2 = \bar{u}_2 &:= \left(\frac{S(-C\alpha_1\lambda_1 + C\alpha_1\lambda_2 + \alpha_2\lambda_1 I - \alpha_2\lambda_2 I)}{2B_2} \right), \\ u_3 = \bar{u}_3 &:= \left(\frac{E(-\lambda_2\sigma_1 - \lambda_2\sigma_2 + \sigma_1\lambda_3 + \sigma_2\lambda_4}{2B_3} \right) \\ u_4 = \bar{u}_4 &= \left(-\frac{I\gamma_1(\lambda_5 - \lambda_3)}{2B_4} \right), \\ u_5 = \bar{u}_4 &= \left(-\frac{C\gamma_1(\lambda_5 - \lambda_4)}{2B_5} \right). \end{aligned}\right\} \quad (12)$$

It suffices to conclude that:

$$\left.\begin{aligned} u_1^* &= \begin{cases} 0, if\ \ \bar{u}_1 \le 0 \\ \bar{u}, if\ \ 0 < \bar{u}_1 < 1 \\ 1,\ if\ \ \bar{u} \ge 1 \end{cases} \\ u_2^* &= \begin{cases} 0, if\ \ \bar{u}_2 \le 0 \\ \bar{u}, if\ \ 0 < \bar{u}_2 < 1 \\ 1,\ if\ \ \bar{u}_2 \ge 1 \end{cases} \\ u_3^* &= \begin{cases} 0, if\ \ \bar{u}_3 \le 0 \\ \bar{u}, if\ \ 0 < \bar{u}_3 < 1 \\ 1,\ if\ \ \bar{u}_3 \ge 1 \end{cases} \\ u_4^* &= \begin{cases} 0, if\ \ \bar{u}_3 \le 0 \\ \bar{u}, if\ \ 0 < \bar{u}_4 < 1 \\ 1,\ if\ \ \bar{u}_4 \ge 1 \end{cases} \\ u_5^* &= \begin{cases} 0, if\ \ \bar{u}_5 \le 0 \\ \bar{u}, if\ \ 0 < \bar{u}_5 < 1 \\ 1,\ if\ \ \bar{u}_5 \ge 1 \end{cases} \end{aligned}\right\} \quad (13)$$

3. 2. Numerical Simulation

We use the Rung kuta scheme embedded in Matlab to numerically simulate the effects of the optimal strategies on the various epidemiological status cum compartments of the model. The results of these simulations are given in Figures 13 to 17. The parameter values used in the simulation are as given in Table 1.

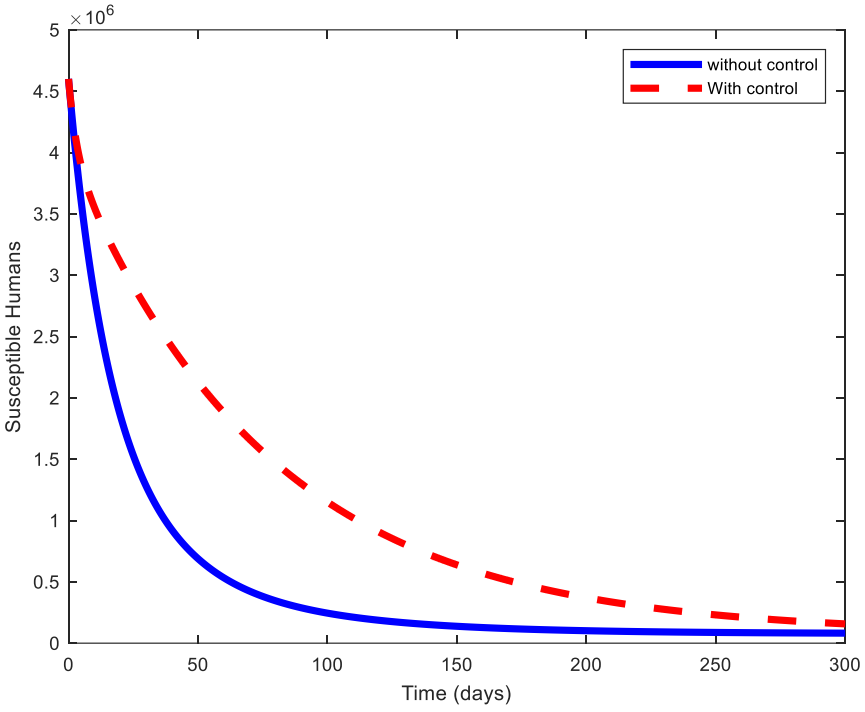

Figure 13. The effect of optimal use of control strategies on the susceptible humans

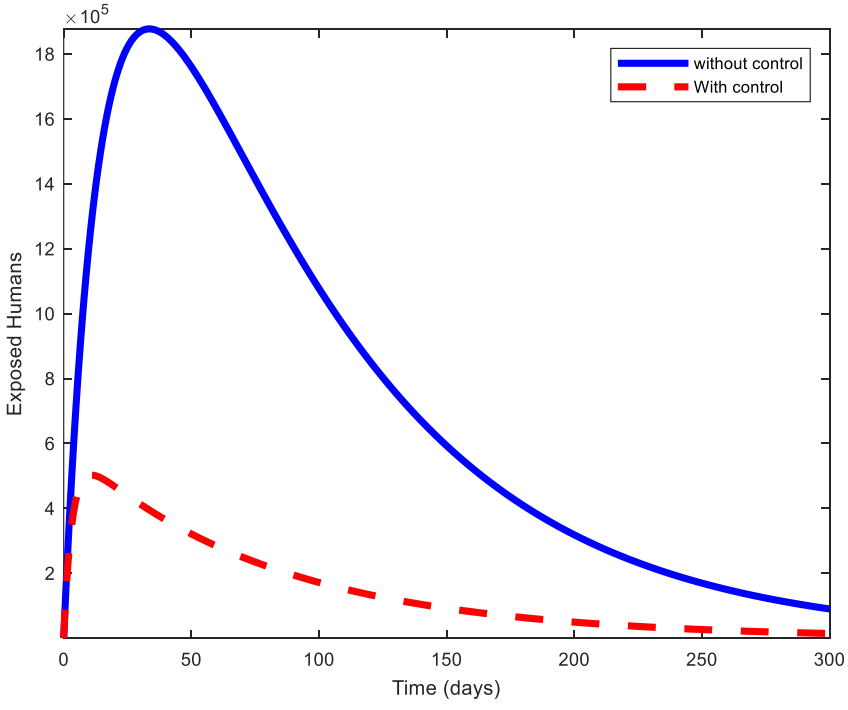

Figure 14. The effect of optimal use of control strategies on the exposed humans

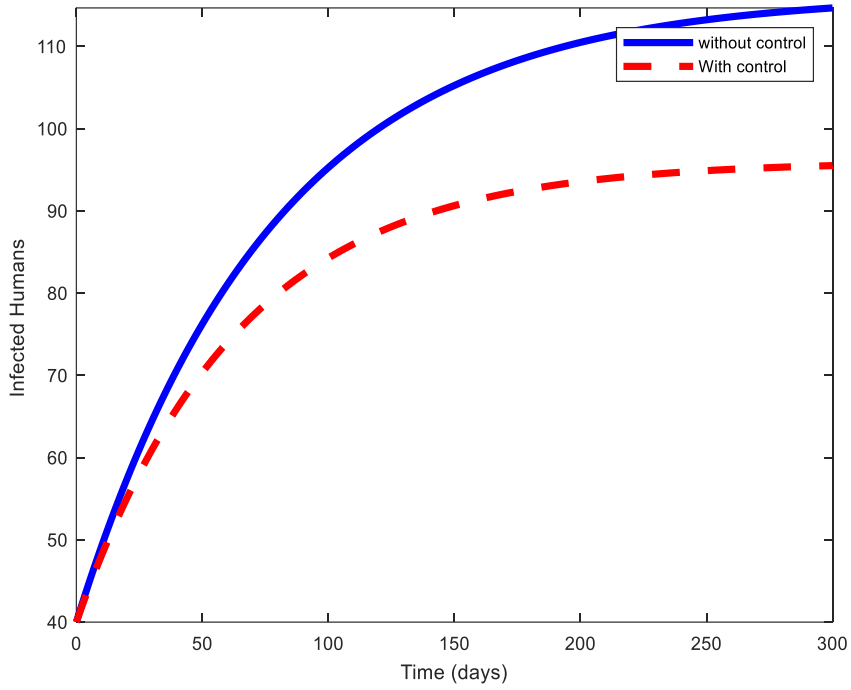

Figure 15. The effect of optimal use of control strategies on the infected humans

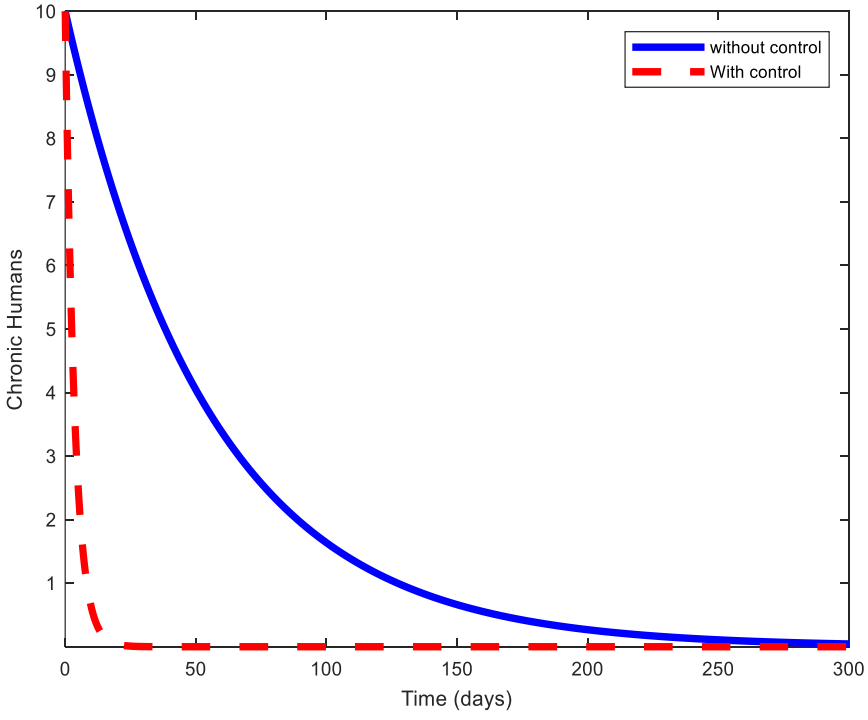

Figure 16. The effect of optimal use of control strategies on the chronically infected humans

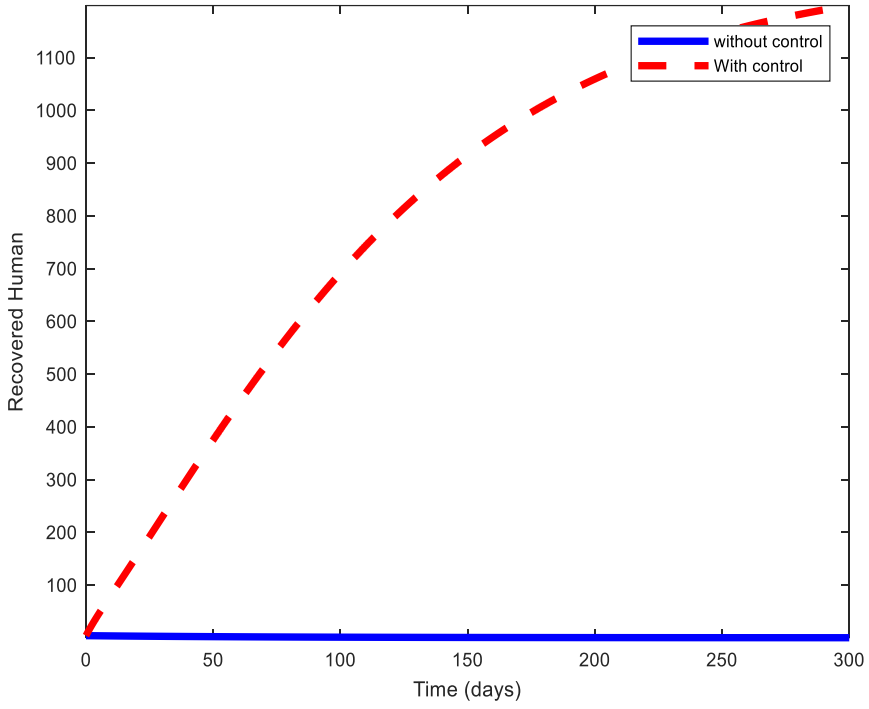

Figure 17. The effect of optimal use of control strategies on the recovered humans

4. CONCLUSIONS

In this paper, we developed and analyzed an ordinary differential equation model for the spread and control of HBV. In the basic model, we considered a population comprising the susceptible, exposed, infected, chronic, and recovered individuals with respect HBV. Firstly, we show that our model (1) is biologically and mathematically well-posed and that all solutions are always positive.

The disease-free and endemic equilibria were obtained, and the most significant threshold in epidemiology (the basic reproductive number) was derived using the next-generation matrix. We conducted a sensitivity analysis of this threshold and extensively juxtaposed it with its various parameters graphically using 4 different values for each parameter in Figures 1 to 13. The transmission rate of acute (infected) individuals, Figure 1, and the recovery rate of chronic individuals, Figure 2, are the most sensitive parameter to the effective reproductive number.

On the other hand, the death rate of infected and chronic individuals (Figures 11 and 12) are the least sensitive parameters to the effective reproductive number. Arising from the sensitivity analysis, we extend the basic model to an optimal control model, which was solved using Pontryagin's principle. As expected, we simulated the control strategies to underscore their effects per time on the various disease dynamics.

The result of the simulation (Figures 13 to 17) shows that if the five controls are in place, HBV will vanish from the population with time. In the feature, we intend to explore the cost-effectiveness of the various controls.

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