



Effect of Control on the Mathematical Model of Hepatitis B Virus with Infective Migrant

Folahan S. Akinboro^{1*}, T. O. Oluyo², O. O. Kehinde³ and S. Alao²

¹*Department of Geomatics, Faculty of Environmental Sciences, University of Benin, Nigeria.*

²*Department of Pure and Applied Mathematics, Faculty of Applied Sciences, Ladoko Akintola University of Technology, Ogbomoso, Nigeria.*

³*Department of Mathematics, University of the Western Cape, Western Cape, South Africa.*

Authors' contributions

This work was carried out in collaboration among all authors. Authors FSA and TOO designed the study, performed the optimal control analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OOK and SA managed the numerical analyses of the study. Author FSA managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ACRI/2020/v20i630202

Editor(s):

(1) Sanjeev Kumar, D. A. V. College, India.

(2) Dr. Tatyana A. Komleva, Odessa State Academy of Civil Engineering and Architecture, Ukraine.

(3) Dr. Imran Aslan, Bingol University, Turkey.

Reviewers:

(1) Ahmed Ali Mohsen, University of Baghdad, Iraq.

(2) Qazi Aftab Kabir, Govt. Gandhi Memorial Science College Jammu, India.

(3) Anal Chatterjee, Barrackpore Rastraguru Surendranath College, India.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/61225>

Original Research Article

Received 15 July 2020
Accepted 22 September 2020
Published 13 October 2020

ABSTRACT

The transmission dynamics of Hepatitis B Virus in a population with infective immigrant is presented with the inclusion of an optimal control strategy to curtail the spread of the virus. To understand the spread of this infection, we develop a mathematical model with control variables of migrant screening and public sensitization. The optimality system is characterized using Pontryagin's maximum principle and solve numerically with an implicit finite difference method. Result of the numerical simulation is presented to illustrate the feasibility of this control strategy. The analysis reveals that combination of both control variables could be the most fruitful way to reduce the incidence of Hepatitis B virus.

*Corresponding author: Email: folahan.akinboro@uniben.edu;

Keywords: *Mathematical model; hepatitis B virus; infective immigrant; Pontryagin's maximum principle; optimal control; finite difference.*

1. INTRODUCTION

It is pathetic that numerous individuals worry more about contracting Acquired Immunodeficiency Syndrome (AIDS) than Hepatitis, even when in reality each year about 600,000 people worldwide die due to these viral hepatitis infections and many more become infected. At times, infected people die faster with viral hepatitis than they would with AIDS. More unfortunate is the fact that Hepatitis B virus is about 50 to 100 times more infectious than HIV [1].

Hepatitis B is a dangerous liver infection brought about by the Hepatitis B Virus which is a significant worldwide medical issue and the most common sort of viral hepatitis. It is endemic in parts of Asia and Africa [2]. Around the world, about 2 billion individuals are asymptomatic or symptomatic of the infection and about 360 million live with the highest degree of infection [3].

In 1990, 154 million individuals or 2.9% of the worldwide populace were migrant, though the comparing figure for 2013 was 3.2% [4] and these numbers exclude undocumented migrant. In 2013, the United States, Canada and some other EU countries were among the 10 top destinations for international migrants [5]. Research on some African migrants in part of the United States showed that the proportion of persons with HBV infection is ten times their host population. This is likely due to a combination of factors, including poor knowledge of the diseases, their risk factors and symptoms, lack of access to healthcare and health information. Studies have shown that workers and displaced people are 2–5 times bound to pass on from liver ailment than their host populace. Based on this submission, it is pertinent to fill the gap in the quest to eradicate HBV infection by presenting a mathematical model which includes treatment class, screening of migrant, adequate sensitization and improvement of public health [6].

The transmission dynamics and control of hepatitis B virus in china was presented by a model, it was reported that HBV is the most common serious viral infection and a leading cause of death in mainland China. Based on the data reported by China Ministry of Health, the model provides an approximate estimate of the

basic reproduction number $R_0 > 2.406$. It was indicated that hepatitis B is endemic in China and is approaching its equilibrium with the current immunization program and control measures. Based on their report, China made great progress in increasing coverage among infants with hepatitis B vaccine thereby reducing the incidence and eventually eradicate the virus [7,8,9]

A mathematical model for hepatitis B with migrant was presented in [10,11]. Analysis showed that strict immigration policies such as screening, and reduction in the number of immigrants into a given population could help control the spread of the disease. The state of art in modeling and interpreting data obtained from hepatitis B virus infected patients treated with antiviral agents was also reviewed in [12]. With increased understanding and quantitative tools, it will be easy to evaluate new treatments for antiviral and immune modulating effects, and may even ultimately predict long-term patient response based on viral kinetic studies.

The role on epidemic models with infective immigrant and vaccination on disease dynamics was explored in [13]. This simple setting considers the possibility of conferred immunity with focus on SIR and SIS models with a vaccinated class. Also, [8,14,15] considered mathematical modeling of infectious diseases. It has shown that combinations of isolation, quarantine, vaccine and treatment are often necessary to eliminate most infectious diseases. However, if they are not administered at the right time and in the adequate amount, the disease elimination will remain a difficult task. With all these findings, our goal is to study the dynamics of Hepatitis B Virus in a population by developing a mathematical model thereby investigating the effects of immigrant and analysing the effect of control variable in reducing HBV incidence.

In Section 2, the state factors, parameters, and the mathematical model for HBV were presented. The control problem is investigated hypothetically and numerically in section 3 while section 4 discusses the results and the conclusion was presented in section 5.

2. FORMULATION OF THE MODEL

A compartmental model for Hepatitis B virus infection is presented with seven compartment:

Susceptible $S(t)$, Latent $L(t)$, Acute $A(t)$, Chronic $C(t)$, Treatment Class $T(t)$, Recovered $R(t)$, and Vaccinated $V(t)$. The treatment class $T(t)$ are set of individuals who are hospitalized or undergoing treatment for the chronic stage of the infection and this is an improvement on the work of Zou et al. [9]. The rates of transfer between the diseases compartments consist of several epidemiological parameters. Recruitment by birth is represented by π , λ represents recruitment by immigration, proportion of birth without vaccination is denoted by ω and $(1-\omega)$ represent birth successfully vaccinated. ρ denotes birth born to carrier mothers i.e Vertically infected birth rate, β represent the transmission rate, k shows the reduced transmission rate from chronic infectiousness to acute infection, μ represent natural death rate for all compartments, δ_1 is the vaccination rate of susceptible population and δ_2 represents loss of immunity of the vaccinated class. The rate at which latent class becomes infectious and progress to acute class is denoted α , i_1 and i_2 are proportion of immigrant with acute and chronic HBV infection respectively, q is the proportion of acute that fails to clear HBV infection and become chronic, γ is the progression rate of acute class, σ represent HBV induced death rate and the rate of flow from chronic to treatment class is ϕ , φ is the rate of progressing from treatment class to recovered class after HBV elimination while $(1-q)$ represents proportion of acute class who cleared the infection and progress to the recovered class.

Then, $\pi\omega(1-\rho C)$ show the new born who are unimmunized and become susceptible, $\pi(1-\omega)$ represents successful immunization of new birth, $\pi\omega\rho C$ measures the new birth who are born to carrier mothers and cannot be vaccinated.

With findings from [16], migrant recruitment term was incorporated into the HBV population model with uninfected immigrant, acutely infected immigrant and chronically infected immigrant where λ represent the recruitment rate for migrant, i_1, i_2 is the proportion of immigrant with acute and chronic infection respectively. Then

$(1-i_1-i_2)$ is the proportion of uninfected or susceptible migrant population.

The transmission dynamics of hepatitis B infection with migrant and treatment class is presented thus:

$$\begin{aligned} S' &= \pi\omega(1-\rho C) + \lambda(1-i_1-i_2) - \beta(A+kC)S - (\mu+\delta_1)S + \delta_2V \\ L' &= \beta(A+kC)S - (\mu+\alpha)L \\ A' &= \lambda i_1 + \alpha L - (\mu+\gamma)A \\ C' &= \lambda i_2 + \pi\omega\rho C + q\gamma A - (\mu+\sigma+\phi)C \\ T' &= \phi C - (\mu+\varphi)T \\ R' &= \varphi T + (1-q)\gamma A - \mu R \\ V' &= \pi(1-\omega) + \delta_1 S - (\mu+\delta_2)V \end{aligned} \tag{1}$$

Subject to initial conditions,

$$S(0) \geq 0, L(0) \geq 0, A(0) \geq 0, C(0) \geq 0, T(0) \geq 0, R(0) \geq 0, V(0) \geq 0.$$

The following assumptions were made:

- (i) The Population is assumed not to be constant since birth, immigration and death occur in the population.
- (ii) The natural death of all classes is the same except for chronic class.
- (iii) The susceptible vaccinated individuals become temporary immune for a period of 25 years.
- (iv) The recovered individuals become permanently immune to the disease for life.
- (v) The chronic infected individual have a diseases induced death rate of σ .
- (vi) This model is assume to be homogeneous mixing of individuals in the population where all individuals have equal likelihood of getting infected if they come in contact with infectious individuals.

2.1 Diseases-Free Equilibrium (DFE)

Consider equation (1), the disease free equilibrium of an epidemic model is obtained by setting

$$\frac{dS}{dt} = \frac{dL}{dt} = \frac{dA}{dt} = \frac{dC}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = \frac{dV}{dt} = 0$$

At disease free equilibrium(DFE), it is assumed that there is no infection, and then all state variables except susceptible and vaccinated are set to be zero [9]. Such that,

$$L = A = C = T = R = 0$$

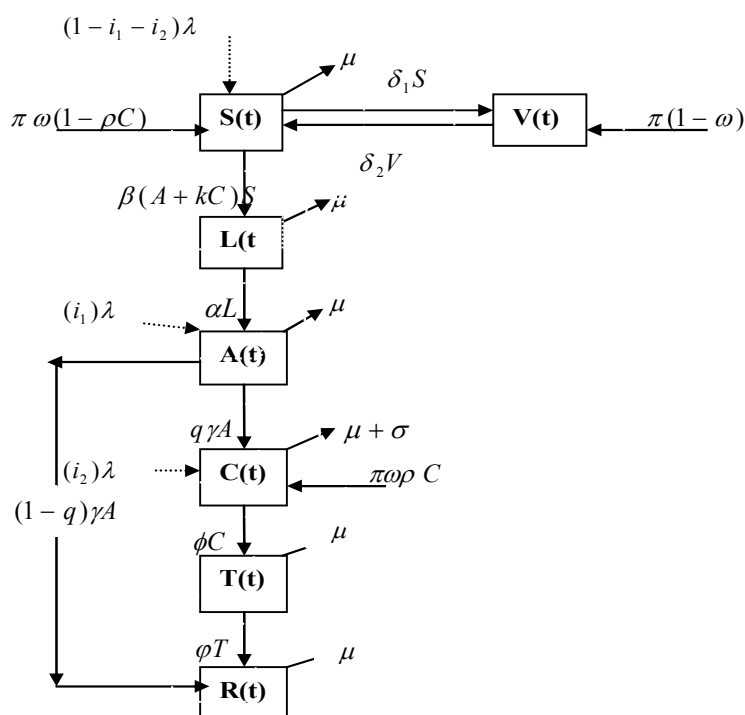


Fig. A. Flow chart for the mathematical model of hepatitis b virus infection with Immigrant

Where S and $V \neq 0$, $S = S_0$ and $V = V_0$

Solving equation (1) at equilibrium,

$$S = S_0, V = V_0, L = A = C = T = R = 0,$$

Then, the DFE of the working model is given as

$$E_0 = (S_0, L_0, A_0, C_0, T_0, R_0, V_0) = \left(\frac{\pi(\mu\omega + \delta_2)}{\mu(\mu + \delta_1 + \delta_2)}, 0, 0, 0, 0, \frac{\pi(\delta_1 + \mu(1-\omega))}{\mu(\mu + \delta_1 + \delta_2)} \right) \quad (2)$$

2.2 Basic Reproduction Number

Basic reproduction number is the effective number of secondary infection caused by an infected individual during his/her period of infectiousness, this makes it an important measure of transmissibility of a disease. Using the next generation matrix operator technique,

the basic reproduction number, R_0 was obtained with mathematical expression [6].

$$R_0 = F_i V_i^{-1}$$

Where F_i is the rate of appearance of new infection in the infected compartment, V_i is the

transfer of individuals out of compartment I by all other means and \mathcal{E}_0 is the disease-free equilibrium. Therefore, the spectral radius of the next generation matrix is the basic reproduction number for the working model [8,11]. Consider equation (1), then

$$F_i = \begin{pmatrix} F_1 \\ F_2 \\ F_3 \end{pmatrix} = \begin{pmatrix} \beta(A+kC)S \\ 0 \\ 0 \end{pmatrix}$$

The jacobian derivative of F is given as

$$\begin{pmatrix} 0 & \beta S_0 & \beta k S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$\text{Where } S_0 = \frac{\pi(\mu\omega + \delta_2)}{\mu(\mu + \delta_1 + \delta_2)}$$

The transfer of individual out of the compartment i is given by

$$V_i = \begin{pmatrix} V_1 \\ V_2 \\ V_3 \end{pmatrix} = \begin{pmatrix} (\mu + \alpha)L \\ (\gamma + \mu)A - \alpha L \\ -\pi\omega\rho C - q\gamma A + (\mu + \sigma + \phi)C \end{pmatrix}$$

Therefore, the jacobian derivative of V_i is

$$V = \begin{pmatrix} \mu + \alpha & 0 & 0 \\ -\alpha & \mu + \gamma & 0 \\ 0 & -q\gamma & \mu + \sigma + \phi - \pi\omega\rho \end{pmatrix}$$

And then equation (5) implies

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu + \alpha} & 0 & 0 \\ \frac{\alpha}{(\mu + \gamma)(\mu + \alpha)} & \frac{1}{\mu + \gamma} & 0 \\ \frac{\alpha q \gamma}{(\mu + \gamma)(\mu + \alpha)(\mu + \sigma + \phi - \pi\omega\rho)} & \frac{q \gamma}{(\mu + \gamma)(\mu + \sigma + \phi - \pi\omega\rho)} & \frac{1}{(\mu + \sigma + \phi - \pi\omega\rho)} \end{bmatrix}$$

Then,

$$FV^{-1} = \begin{pmatrix} 0 & \beta S_0 & \beta k S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} * \begin{bmatrix} \frac{1}{\mu + \alpha} & 0 & 0 \\ \frac{\alpha}{(\mu + \gamma)(\mu + \alpha)} & \frac{1}{\mu + \gamma} & 0 \\ \frac{\alpha q \gamma}{(\mu + \gamma)(\mu + \alpha)(\mu + \sigma + \phi - \pi\omega\rho)} & \frac{q \gamma}{(\mu + \gamma)(\mu + \sigma + \phi - \pi\omega\rho)} & \frac{1}{(\mu + \sigma + \phi - \pi\omega\rho)} \end{bmatrix}$$

$$\Rightarrow FV^{-1} = \begin{bmatrix} M & N & P \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Then, the basic reproduction number is the dominant eigenvalue of FV^{-1} ,

$$R_0 = \frac{\beta S_0 \alpha}{(\mu + \alpha)(\mu + \gamma)} + \frac{\beta k S_0 \alpha q \gamma}{(\mu + \alpha)(\mu + \gamma)(\mu + \sigma + \phi - \pi\omega\rho)} \quad (3)$$

From the above, the basic reproduction number R_0 is the largest eigenvalue of the working model and defined as the effective number of secondary infection caused by an infected individual during his/her period of infectiousness [11].

2.3 Optimal Control of HBV Model with Immigrant

In this work, we are concerned with the problem of adopting the best strategy of controlling the spread of hepatitis in the presented mathematical model with immigrants; that is, we seek to search a maximum count of uninfected population with a minimum cost of the control strategy. Hepatitis model of equation (1) was extended to include two time dependent controls. These two major controls are screening of immigrants and public awareness are incorporated in the model to reduce the contact/ transmission rate. The purpose of this control strategy is to minimize the

number of infected individuals and maximizing the number of uninfected individuals. [7,15].

For this analysis all control variable are constrained between zero and one, this implies that when the control value is one the maximum control effort is invested and when the control is set at zero then no control effort is invested.

Hence, we denote $u_1(t)$ as screening of immigrant control variable and $u_2(t)$ as sensitization control variable, the optimal control system is given by:

$$\begin{aligned} \frac{dS}{dt} &= \pi\omega(1 - \rho C) + \lambda(1 - i_1 - i_2)(1 - u_1(t)) - (1 - u_2(t))\beta(A + kC)S - (\mu + \delta_1)S + \delta_2 V \\ \frac{dL}{dt} &= (1 - u_2(t))\beta(A + kC)S - (\mu + \alpha)L \\ \frac{dA}{dt} &= \lambda i_1(1 - u_1(t)) + \alpha L - (\mu + \gamma)A \\ \frac{dC}{dt} &= \lambda i_2(1 - u_1(t)) + \pi\omega\rho C + q\gamma A - (\mu + \sigma + \phi)C \\ \frac{dT}{dt} &= \phi C - (\mu + \varphi)T \\ \frac{dR}{dt} &= \varphi T + (1 - q)\gamma A - \mu R \\ \frac{dV}{dt} &= \pi(1 - \omega) + \delta_1 S - (\mu + \delta_2)V \end{aligned} \quad (4)$$

The objective functional of the optimal control system is given as

$$J = \max_{u \in U} \int_{t_0}^{t_f} (S(t) - [D_1 u_1^2 + D_2 u_2^2]) dt \quad (5)$$

The objective functional [8,14] is defined to maximize the benefit based on the immune population and minimizing the cost based on implementing this control. The parameters $D_1 \geq 0$ and $D_2 \geq 0$ represent the weights on the benefit and cost and t_f is the final time.

The optimal control for (u_1^*, u_2^*) is given such that

$$J(u_1^*, u_2^*) = \max_{u_1, u_2 \in U} J(u, u_2)$$

Where,

U is the set of measurable function defined from $[0, t_f]$ to $[0, 1]$. For $(S(t), L(t), A(t), C(t), R(t), T(t), V(t))$ subject to the state equation and the initial conditions;

$$S(0)=S_0, L(0)=L_0, A(0)=A_0, C(0)=C_0, T(0)=T_0, R(0)=R_0, V(0)=V_0$$

Are free where D_i , for $i=1..2$ are positive constant that are represented to keep a balance of the size of $S(t), L(t), A(t), C(t), R(t), T(t), V(t)$.

D_1 and D_2 are weight corresponding to the controls u_1 and u_2 respectively. U_{max} is the maximum attainable value for controls

$$u_{1max} \text{ and } u_{2max} \tag{6}$$

Where u_{1max} and u_{2max} depend on the amount of resources available to implement each control measure.

2.4 Optimality System

Pontryagin's maximum principle is a necessary condition that an optimal control [15] must satisfy. This principle is used in the characterization of an optimal control problem.

To find an optimal solution pair, we firstly define the langrangian of the problem as

$$L(S, L, A, C, T, R, V, u_1, u_2) = [S(t) - (D_1 u_1^2 + D_2 u_2^2)] \tag{7}$$

The pontryagin's maximum principle is used in equation (7) to analyze the maximum langrangian of the optimality system. This principle convert both the objective functional and the optimal control pair in a problem of maximizing point wise a Hamiltonian H with respect to u_1, u_2 . If $u^*(t)$ and $x^*(t)$ are optimal, there exist an adjoint variable $\lambda(t)$ such that :

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t))$$

At each time for all u where Hamitonian is defined by

$$H(t, x(t), u(t), \lambda(t)) = f(t, x(t), u(t)) + \lambda(t)g(t, x(t), u(t))$$

$$\lambda(t) = - \frac{\partial H(t, x(t), u(t), \lambda(t))}{\partial x}$$

Where $\lambda(T)=0$

Using PMP to find the optimal control equation through the adjoint variable [14,15,17],the Hamitonian is defined as the integrand of the objective function couple with the right hand side of the state

$$\lambda_s(t), \lambda_L(t), \lambda_A(t), \lambda_C(t), \lambda_T(t), \lambda_R(t), \lambda_V(t)$$

The Hamiltonian for this problem is define as:

$$H(S, L, A, C, T, R, V, u_1, u_2, \lambda_s, \lambda_L, \lambda_A, \lambda_C, \lambda_T, \lambda_R, \lambda_V) = L + \lambda_s \frac{dS}{dt} + \lambda_L \frac{dL}{dt} + \lambda_A \frac{dA}{dt} + \lambda_C \frac{dC}{dt} + \lambda_T \frac{dT}{dt} + \lambda_R \frac{dR}{dt} + \lambda_V \frac{dV}{dt}$$

Theorem 1

An optimal control pair u_1^*, u_2^* and solutions $S^*, L^*, A^*, C^*, T^*, R^*, V^*$ of the corresponding state system (4), there exist adjoint variable $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7$ satisfying

$$\begin{aligned} \dot{\lambda}_s &= -1 + (1 - u_2(t))\beta(A + kC)(\lambda_s - \lambda_L) + (\mu + \delta_1)\lambda_s - \delta_1\lambda_V \\ \dot{\lambda}_L &= \mu\lambda_L + \alpha(\lambda_L - \lambda_A) \\ \dot{\lambda}_A &= (1 - u_2(t))\beta S(\lambda_s - \lambda_L) + (\gamma + \mu)\lambda_A - q\gamma\lambda_C - (1 - q)\gamma\lambda_R \\ \dot{\lambda}_C &= \pi\omega\rho(\lambda_s - \lambda_C) + (1 - u_2(t))k\beta S(\lambda_s - \lambda_L) + (\mu + \sigma)\lambda_C + \phi(\lambda_C - \lambda_T) \\ \dot{\lambda}_T &= \phi(\lambda_T - \lambda_R) + \mu\lambda_T \\ \dot{\lambda}_R &= \mu\lambda_R \\ \dot{\lambda}_V &= \delta_2(\lambda_V - \lambda_s) + \mu\lambda_V \end{aligned}$$

With transversality condition

$$\lambda_s(t_{final}) = \lambda_L(t_{final}) = \lambda_A(t_{final}) = \lambda_C(t_{final}) = \lambda_T(t_{final}) = \lambda_R(t_{final}) = \lambda_V(t_{final}) = 0$$

$$u_1^*(t) = \min \left\{ \max \left\{ 0, \frac{i_1 \lambda(\lambda_s - \lambda_A) + i_2 \lambda(\lambda_s - \lambda_C)}{2D_1} \right\}, 1 \right\}$$

$$u_2^*(t) = \min \left\{ 0, \max \left\{ 0, \frac{(\beta(A + kC)S)(\lambda_L - \lambda_s)}{2D_2} \right\}, 1 \right\}$$

Proof

The adjoint system can be determined by differentiating the Hamiltonian with respect to variables of the control problem. With transversality conditions

$$\lambda_s(t_{final}) = \lambda_L(t_{final}) = \lambda_A(t_{final}) = \lambda_C(t_{final}) = \lambda_T(t_{final}) = \lambda_R(t_{final}) = \lambda_V(t_{final}) = 0$$

Using the optimality condition, the langrangian is maximized with respect to the set of controls at optimal (u_1^*, u_2^*) .

$$\text{Then } \left. \frac{\partial H}{\partial u} \right|_{u=(u_1^*, u_2^*)} = 0$$

The hamitonian (H) is given as

$$H = -(D_1 u_1^2 + D_2 u_2^2) - [\lambda(i_1 + i_2)(1 - u_1(t)) - (1 - u_2(t))\beta(A + kC)S] \lambda_s + (1 - u_2(t))\beta(A + kC)S \lambda_L + (1 - u_1(t))i_1 \lambda_A + (1 - u_1(t))i_2 \lambda_C$$

Then, for u_1 :

$$\frac{dH}{du_1} = -2D_1 u_1 + \lambda(i_1 + i_2)\lambda_s - i_1 \lambda_A - i_2 \lambda_C \quad \text{at } u_1 = u_1^*$$

$$\frac{dH}{du_1} = -2D_1 u_1^* + i_1 \lambda(\lambda_s - \lambda_A) + i_2 \lambda(\lambda_s - \lambda_C)$$

$$\text{Maximizing the langrangian, set } \frac{dH}{du_1} = 0,$$

For control u_2 , the hamiltonian (H):

$$H = -(D_1 u_1^2 + D_2 u_2^2) - [\lambda(i_1 + i_2)(1 - u_1(t)) - (1 - u_2(t))\beta(A + kC)S] \lambda_s - (1 - u_2(t))\beta(A + kC)S \lambda_L + (1 - u_1(t))i_1 \lambda_A + (1 - u_1(t))i_2 \lambda_C$$

$$\frac{dH}{du_2} = -2D_2 u_2 - (\beta(A + kC)S)\lambda_s + \beta(A + kC)S \lambda_L \quad \text{at } u_2 = u_2^*$$

Then, the two controls are bounded by 1 and 0 which are the lower and upper bounds respectively, that is

$$u_1^* = \begin{cases} 0 & \text{if } \bar{u}_1 \leq 0 \\ \bar{u}_1 & \text{if } 0 < \bar{u}_1 < 1 \\ 1 & \text{if } \bar{u}_1 \geq 1 \end{cases}$$

This can be written in compact notion as

$$u_1^*(t) = \min \left\{ \max \left\{ 0, \frac{i_1 \lambda(\lambda_s - \lambda_A) + i_2 \lambda(\lambda_s - \lambda_C)}{2D_1} \right\}, 1 \right\}$$

And for the second control function,

$$u_2^* = \begin{cases} 0 & \text{if } \bar{u}_2 \leq 0 \\ \bar{u}_2 & \text{if } 0 < \bar{u}_2 < 1 \\ 1 & \text{if } \bar{u}_2 \geq 1 \end{cases}$$

Hence, the second control function can also be written as,

$$u_2^*(t) = \min \left\{ 0, \max \left\{ 0, \frac{(\beta(A + kC)S)(\lambda_L - \lambda_s)}{2D_2} \right\}, 1 \right\}$$

From the above, then

$$u_1^* = \min \left\{ \max \left\{ 0, \frac{i_1 \lambda(\lambda_s - \lambda_A) + i_2 \lambda(\lambda_s - \lambda_C)}{2D_1} \right\}, 1 \right\}$$

$$u_2^* = \min \left\{ 0, \max \left\{ 0, \frac{(\beta(A + kC)S)(\lambda_L - \lambda_s)}{2D_2} \right\}, 1 \right\} \quad (8)$$

Remark 1: The optimality system [8] is given below by incorporating the optimal control pair in the state system coupled with the adjoint system. Thus,

$$\lambda_s(t_f) = \lambda_L(t_f) = \lambda_A(t_f) = \lambda_C(t_f) = \lambda_T(t_f) = \lambda_R(t_f) = \lambda_V(t_f) = 0 \text{ and } S(0) = S_0, L(0) = L_0, A(0) = A_0, C(0) = C_0, T(0) = T_0, R(0) = R_0, V(0) = V_0$$

By theorem (1), hence the solution of optimality system exists.

The controls are characterized in terms of the unique solution of the optimality system. Then, equation (8) gives an optimal control strategy for Hepatitis B Virus under the scenario of these two control strategies (u_1^* and u_2^*).

2.5 Numerical Analysis for the Control Problem

The optimality system is solved using finite difference method with iterative scheme for the state variables forward in time and the adjoint variable backward in time. The control variables are updated at the end of each iteration using the

calculated optimal control value u_1^*, u_2^* . In this section, we observe the effect of controls introduced to eradicate or reduce the spread of hepatitis B virus.

The optimality system is solved using a finite-difference method where the interval t_0, t_f is discretized at the point $t_k = ml + t_0$ ($m = 0, 1, \dots, n$), where l is the time step. Next, we define the state and adjoint variables.

$$S(t), L(t), A(t), C(t), T(t), R(t), V(t), \lambda_s, \lambda_L, \lambda_A, \lambda_C, \lambda_T, \lambda_R, \lambda_V$$

and the controls $u_1(t), u_2(t)$ in terms of nodal points

$$S^k, L^k, A^k, C^k, T^k, R^k, V^k, \lambda^k_s, \lambda^k_L, \lambda^k_A, \lambda^k_C, \lambda^k_T, \lambda^k_R, \lambda^k_V, u_1^k, u_2^k$$

with

$$S^0, L^0, A^0, C^0, T^0, R^0, V^0, \lambda^0_s, \lambda^0_L, \lambda^0_A, \lambda^0_C, \lambda^0_T, \lambda^0_R, \lambda^0_V, u_1^0, u_2^0$$

at initial time t_0 .
 $S^n, L^n, A^n, C^n, T^n, R^n, V^n, \lambda^n_s, \lambda^n_L, \lambda^n_A, \lambda^n_C, \lambda^n_T, \lambda^n_R, \lambda^n_V, u_1^n, u_2^n$

at final time t_f . The time derivative of first-order forward-difference [5] is given for the state variable as

$$\begin{aligned} \frac{dS}{dt} &= \lim_{h \rightarrow 0} \frac{S(t+h) - S(t)}{h} \\ \frac{dL}{dt} &= \lim_{h \rightarrow 0} \frac{L(t+h) - L(t)}{h} \\ \frac{dA}{dt} &= \lim_{h \rightarrow 0} \frac{A(t+h) - A(t)}{h} \\ \frac{dC}{dt} &= \lim_{h \rightarrow 0} \frac{C(t+h) - C(t)}{h} \\ \frac{dT}{dt} &= \lim_{h \rightarrow 0} \frac{T(t+h) - T(t)}{h} \\ \frac{dR}{dt} &= \lim_{h \rightarrow 0} \frac{R(t+h) - R(t)}{h} \\ \frac{dV}{dt} &= \lim_{h \rightarrow 0} \frac{V(t+h) - V(t)}{h} \end{aligned} \tag{9}$$

To solve equation (9), the scheme improved by Karrakchou [7] was adopted to solve this case

$$\begin{aligned} \frac{S^{m+1} - S^m}{h} &= \pi v - \pi v p C^m + \lambda(1 - i_1 + i_2)(1 - u_1^m) - (1 - u_2^m) \beta(A^m + KC^m) S^{m+1} - (\mu + \delta) S^{m+1} + \delta V^m \\ \frac{L^{m+1} - L^m}{h} &= (1 - u_2^m) \beta(A^m + KC^m) S^{m+1} - (\mu + \alpha) L^{m+1} \\ \frac{A^{m+1} - A^m}{h} &= \lambda i_1 (1 - u_1^m) + \alpha L^{m+1} - (\mu + \gamma) A^{m+1} \\ \frac{C^{m+1} - C^m}{h} &= \lambda i_2 (1 - u_1^m) + \pi v p C^{m+1} + q A^{m+1} - (\mu + \sigma + \phi) C^{m+1} \\ \frac{T^{m+1} - T^m}{h} &= \phi C^{m+1} - (\mu + \phi) T^{m+1} \\ \frac{R^{m+1} - R^m}{h} &= \phi A^{m+1} + (1 - q) A^{m+1} - \mu R^{m+1} \\ \frac{V^{m+1} - V^m}{h} &= \pi(1 - v) + \delta S^{m+1} - (\mu + \delta) V^{m+1} \end{aligned} \tag{10}$$

We couple equation (9) and (10) to establish an algorithm where

$$R_1^k = \frac{i_1 \lambda (\lambda_S^{n-m-1} - \lambda_A^{n-m-1}) + i_2 \lambda (\lambda_S^{n-m-1} - \lambda_C^{n-m-1})}{2D_1}$$

$$R_2^k = \frac{\beta(A^{m+1} + KC^{m+1}) S^{k+1} (\lambda_L^{n-m-1} - \lambda_C^{n-m-1})}{2D_2}$$

$$u_1^{m+1} = \min(1, \max(R_1, 0)) \text{ and}$$

$$u_2^{m+1} = \min(1, \max(R_2, 0))$$

Hence, the above algorithm is computed using maple software for the coupled system of State, Adjoint and Control variable with given initial condition below and parameters in Table 1

$$S(0) = S_0, L(0) = L_0, A(0) = A_0, C(0) = C_0, T(0) = T_0, R(0) = R_0, V(0) = V_0,$$

3. RESULTS AND DISCUSSION

The value of the basic reproduction number is calculated by substituting the parameters listed in Table 1 into equation (3) which gives $R_0 = 1.0925$. The optimality system was analyzed numerically using implicit finite difference method with iterative scheme for the state variables forward in time and the adjoint variable backward in time. The control variables are updated at the end of each iteration using the calculated optimal control value u_1^*, u_2^* . Graphical illustrations presented shows the disease progression with the independent variable (t) on the x-axis and the state variables on the y-axis.

The result of the optimal control model is discussed using the two time dependent control variable $u_1(t), u_2(t)$, screening of immigrant $u_1(t)$ and sensitization $u_2(t)$ to investigate the effect of the combination of this controls on the transmission dynamics of HBV as observed in Figs 1-7. We observed in Fig. 1 that the susceptible population has a higher number of individuals compared with the uncontrolled case which is as a result of effectiveness of the control and led to a reduction in the transmission rate β and infective immigrant i_1, i_2 thereby reducing the incidence of the virus. This claim is in agreement with the discussion in [9].

It was observed from Figs. 2, 3 and 4 that the combination of controls resulted in significant reduction in the number of latent, acute and chronic population as against the increasing number of infectives in the uncontrolled model.

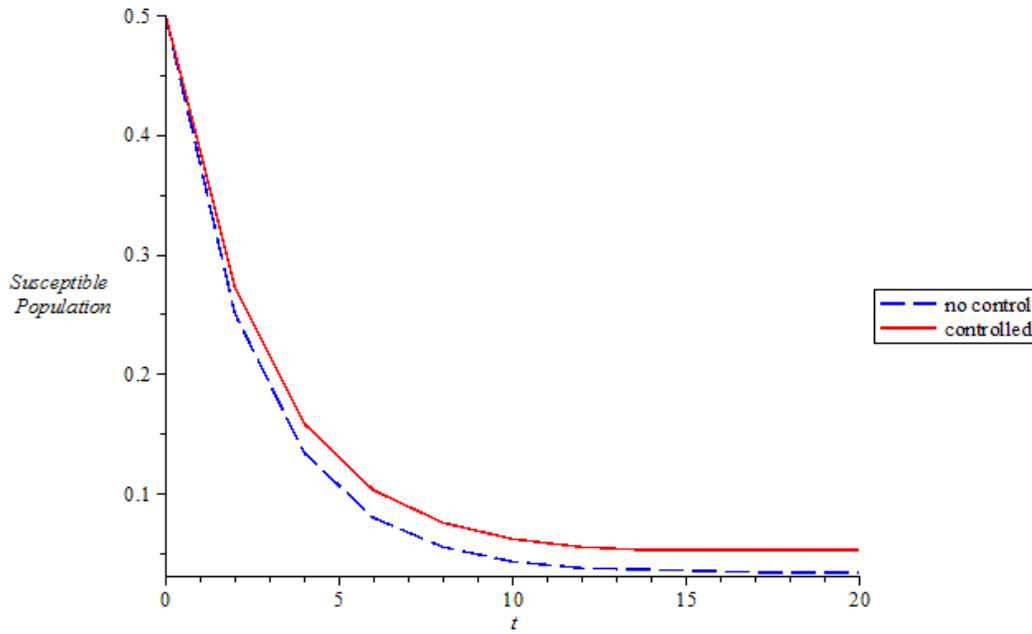


Fig. 1. Impact of control on Susceptible class against time (t)

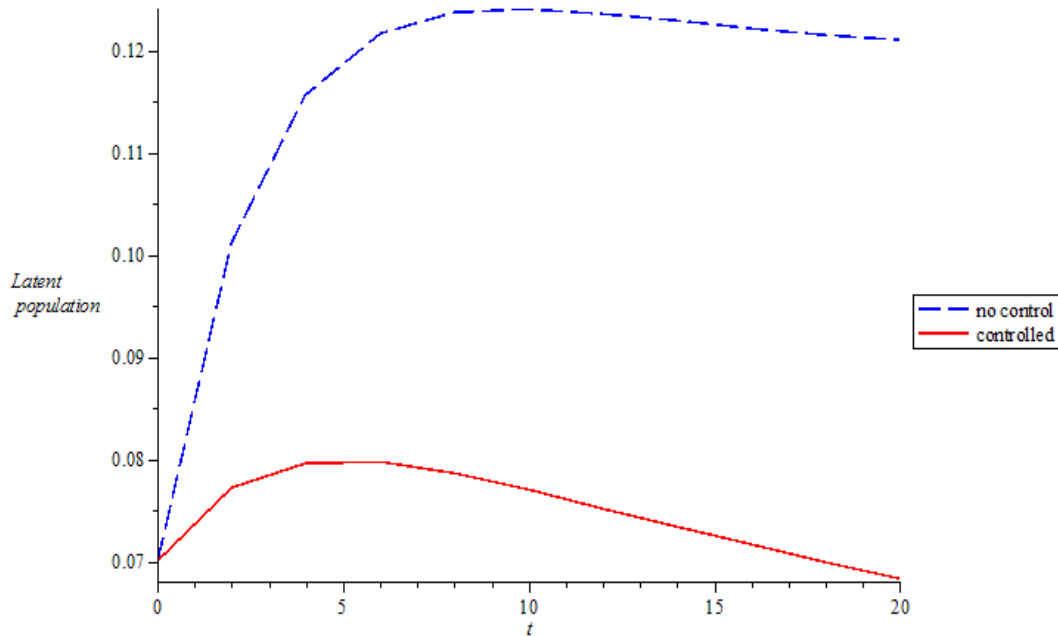


Fig. 2. Impact of control on Latent class against time (t)

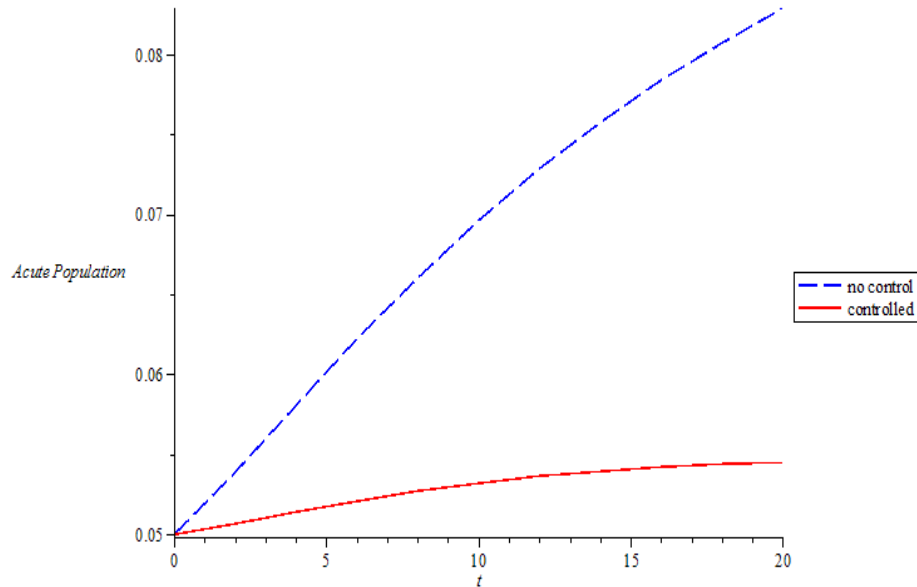


Fig. 3. Impact of control on Acute class against time (t)

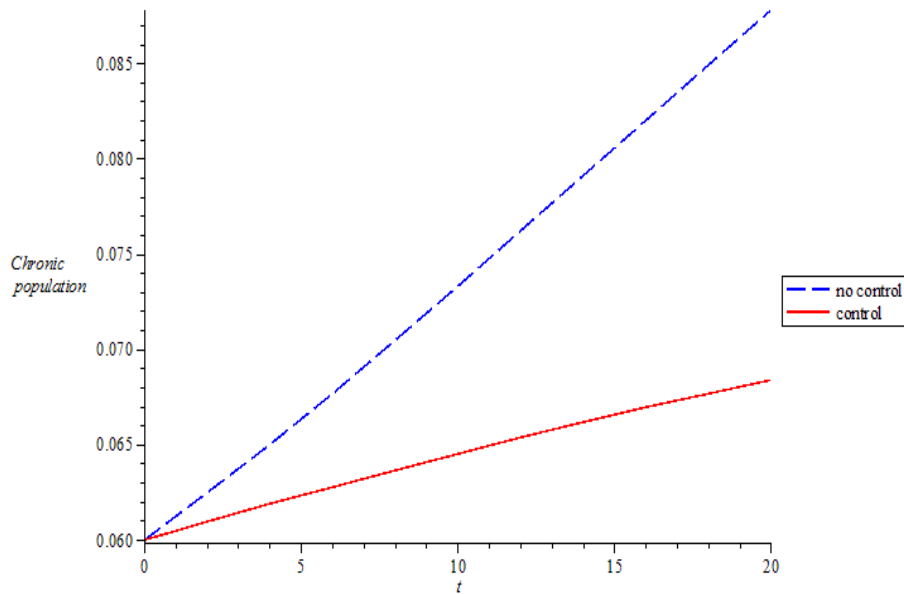


Fig. 4. Impact of control on Chronic class against time (t)

Figs. 5 and 6 explain the role of control pair $u_1(t), u_2(t)$ on treatment and recovered class. Experimentally, $u_2(t)$ reduced the transmission of HBV while $u_1(t)$ prevent infective migrants from entering the population which resulted in a lower number of infected individual to undergo treatment. Fig. 7 show the effect

of control on vaccinated class against time (t). It was observed that the vaccinated population for both controlled and uncontrolled model increases due to presence of intervention strategies while the controlled model of case 3 has a higher vaccinated population compared with the uncontrolled cases.

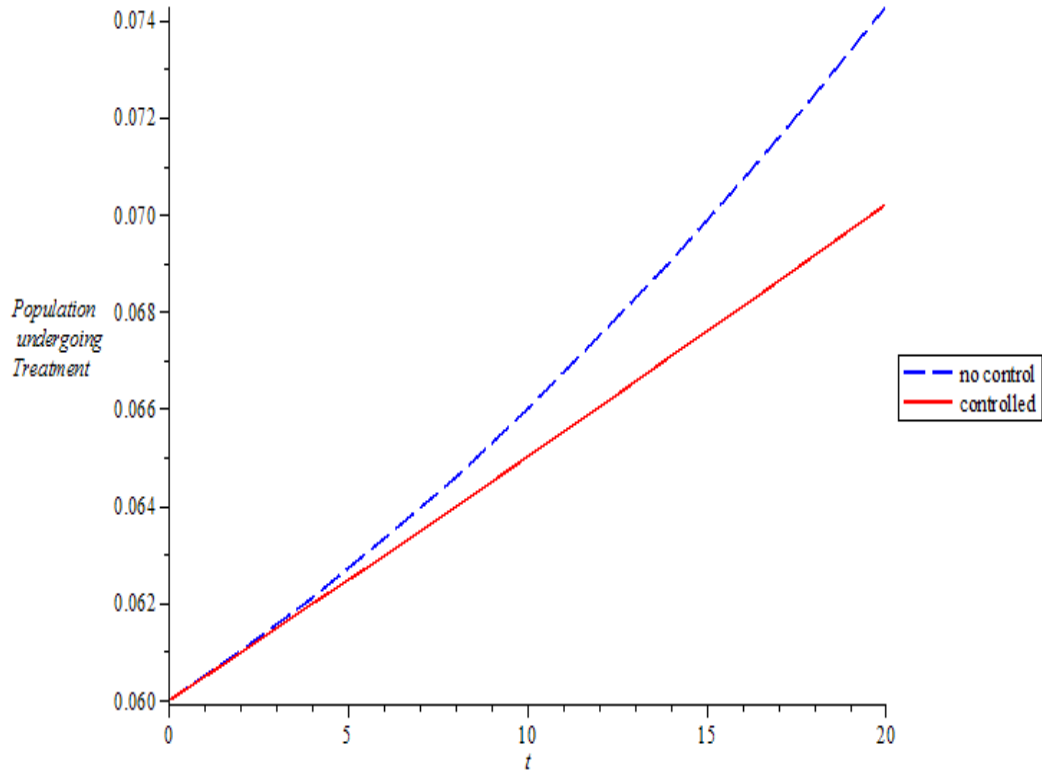


Fig. 5. Impact of control on treatment class against time (t)

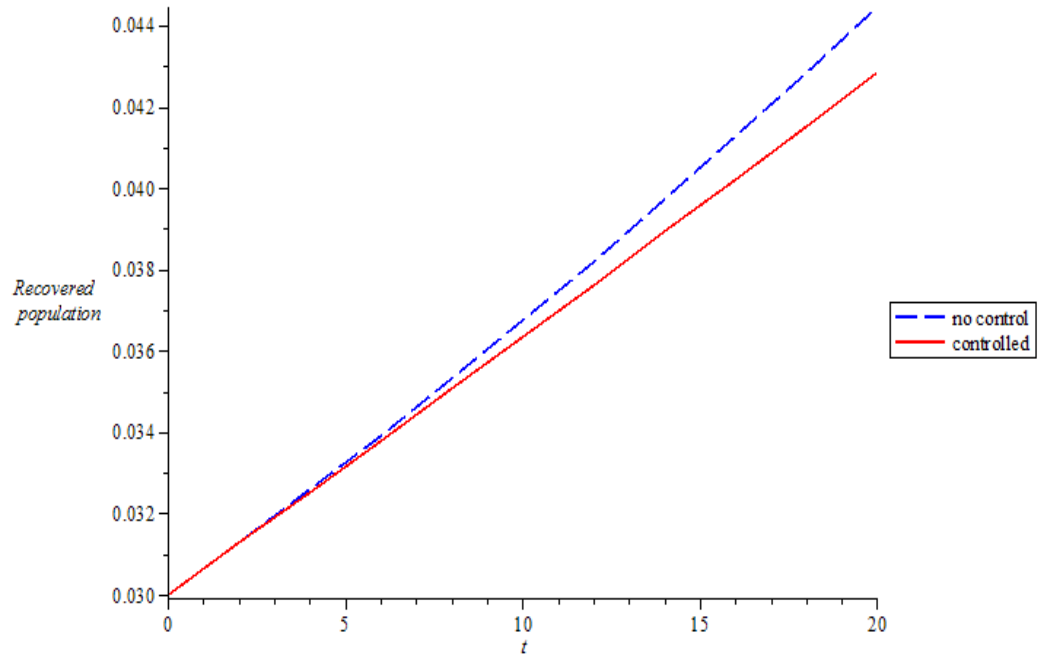


Fig. 6. Impact of control on Recovered class against time (t)

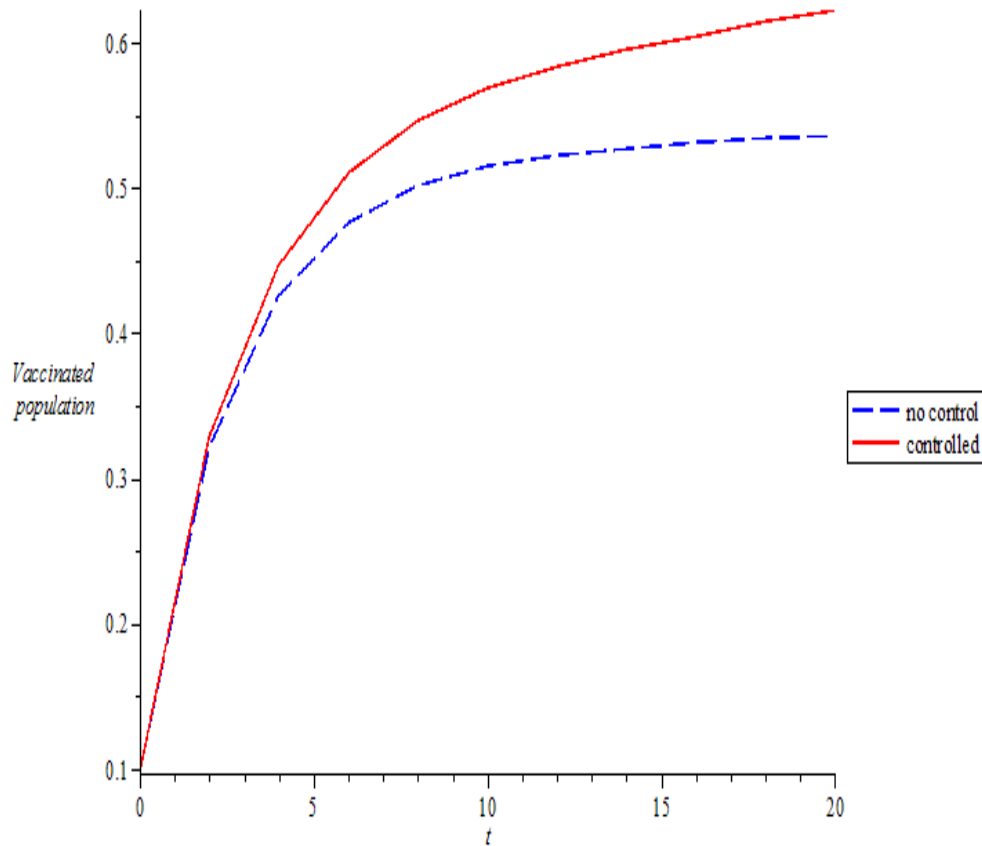


Fig. 7. Impact of control on Vaccinated class against time (t)

Table 1. Summary of parameter values used in Figures

Parameter	Value	Source
β	0.8	[11]
k	0-1, 0.16/year	[18]
π	0.0143/year	[11]
ρ	0.7/year	[11]
ω	0-1/year	[9]
μ	0.0121, 0.00693/year	[9]
σ	0.002/year	[9]
δ_1	0.3/year	[11]
δ_2	0.1/year	[9]
α	6/year	[11]
q	0.285/year	[9]
γ	0.3/year	[11]
$1-q$	0.1-0.95, 0.715	[9]
ϕ	0.025/year	Estimated
φ	0.01/year	Estimated

4. CONCLUSION

The simulation of the presented mathematical model with the two control pair u_1 and u_2 reduced the prevalence of HBV in a dynamic population. Also, the inclusion of treatment class in the model revealed reduction in endemicity and transmission of the disease. From this work, the combination of the two controls screening of immigrant $u_1(t)$ and adequate sensitization of the public $u_2(t)$ plays an important role in eradicating the infection. Routine screening of migrants and refugees for viral hepatitis should be performed in majority of host nations since multiple studies suggest that screening of migrants is likely to be cost-effective, especially in the case of HBV. In order to lower the transmission/contact rate of HBV, sensitization on Hepatitis B Virus modes of infection should be organized for health workers and the populace at large.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. WHO (World Health Organization). Hepatitis B vaccines. WHO position paper. Wkly Epidemiol. 2004;79:255–263.
2. WHO (World Health Organization). National Hepatitis B Needs Assessment; 2008.
3. Williams R. Global Challenges In Liver Disease, Journal of Hepatology. 2006; 44(3):521–526.
4. Ahmed F, Foster GR. Global Hepatitis, Migration and its Impact on Western Healthcare, Baij Group Ltd and British Soc. of Gastroenterology. 2010;59(8):1009–1011..
5. Galbrain JW, Donnell JP, Franco R, Overton T, Rodgersm JB, Wang HE. National estimates of healthcare utilization by individuals with hepatitis C virus infection in the United States, Clin. Infect Dis. 2014;59(6):755–764.
6. Lequam M. A Mathematical Model Of The Dynamics For Anti-HBV Infection Treatment with Peginterferon Alfa-2a, J. Tempe. 2008;1433-1436.
7. Gaff H, E Schaefer. Optimal control applied to vaccination and treatment strategies for various epidemiological models, Mathematical biosciences and engineering. 2009;6:460-492.
8. Zhang J, Zhang S. Application and Optimal Control for an HBV Model with Vaccination and Treatment, Hindawi Discrete Dynamics in Nature and Society. 2018; 2018:1-13.
9. Zou L, Zhang W, Ruan S. Modeling the transmission dynamics and control of hepatitis B virus in China, Journal of Theoretical Biology. 2010;262:330–338.
10. Mohammed ID, Baba S. Modeling the effect of Irresponsible infective immigrants on the transmission dynamics Of HIV/Aids, International Research Publication House. ISSN 2248-9983. 2012; 3(1):31-40.
11. Mohammad RM, Tayebah W. A Mathematical Model for HBV, J. Basic. Appl. Sci. Res. 2012;2(9):9407-9412.
12. Ruy MR, Arthur L, Alan SP. Dynamics Of hepatitis B virus Infection, J. Microbes AND Infection, 2002;4:829–835.
13. Shim E. An epidemic model with infective immigrants and vaccination. M.Sc Thesis, University of British Columbia, Vancouver, BC, Canada; 2004
14. Sharomi O, Malik T. Optimal control in epidemiology, Annual operation research. 2015;227-1834-4.
15. Khan T, Zaman G, Chohan MI. The transmission dynamic and optimal control of acute and chronic hepatitis B, Journal of biological dynamics. 2017;11(1);172–189.
16. Brauer F, Castillo-Chavez C. Mathematical Models in Population Biology and Epidemiology, New York: Springer-Verlag; 2001.
17. Karrakchou J, Rachik M, Gourari S. Optimal control and infectiology: Application of HIV/AIDS model, J. Applied mathematics and computation. 2006;177:807-818.
18. Pang J, Cui JA, Zhou X. Dynamical behavior of a hepatitis B virus transmission model with vaccination. Journal of Theoretical Biology. 2010;265(4):572-8.

© 2020 Akinboro et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/61225>*