Dynamics of Hepatitis B Virus Disease with Infectious Latent and Vertical Transmission

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Abstract: - Hepatitis B has become a major health threat because it is a life-threatening liver disease with an estimated 0.25 billion people suffering from this infectious disease worldwide. This paper presents a SLITR (Susceptible-Latent-Infectious-Treatment-Recovery) mathematical model that combines both vaccination and treatment as a means of controlling the hepatitis B virus (HBV). The nonlinear ordinary differential equations for the HBV transmission capacities were resolved and the basic reproduction number R_o computed using the next generation matrix method and simulated numerically using the Runge-Kutta fourth order scheme implemented using MatLab. The stability points for disease-free equilibrium state (DFE), endemic equilibrium state (EE), and basic reproduction number R_0 were obtained and the results show that the disease-free equilibrium was both locally and globally asymptotically stable $(R_0 < 1)$. Similarly, treatment or vaccine administered was effective in alleviating the spread of HBV disease, and when both control strategies are combined, the diseases are quickly controlled and eventually eradicated.

Key-Words: - HBV, Disease, Latent, Vertical transmission, Infectious, Stability.

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1 Introduction

A very large variety of organisms exist, including some which can survive and find the bodies of people or animals suitable for their development, and These organisms are an infectious agent (also called pathogens) which causes infection and illness through the toxins produced are communicable and infectious. Waste products from the host, be it faeces or urine (latency and persistence) develops within the environment or intermediate host before making contact with a susceptible person or animal, [1], [2]. Pathogens are non-infectious during the latent period but non-latent pathogens are infectious directly after excretion, [3]. Infected persons transmit this virus vertically either before or after birth from an infected mother to the newborn or through the body fluid of an infected person to an uninfected person via sharing of non-sterilized injection syringes, tattoo materials, and through sex, among others.

Viral hepatitis, an inflammation of the liver is caused by one or more of five main hepatic viruses: A, B, C, D, and E. These viruses exhibit similar symptoms that can potentially cause liver disease to varying degrees; they however differ significantly in regards to epidemiology, prevention, diagnosis, care, and treatment. This virus is categorized as a major global health problem with over 400 million patients chronically infected, with death cases of > 1.4 million deaths per year, [4]. Nigeria is known to be among the countries with a high affliction of viral hepatitis with a Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) prevalence of 11% and

2.2%, [5]. Statistics show that there are over 350 million chronic carriers of HBV with 6 million deaths per year due to HBV related liver disease or hepatocellular carcinoma and this has become a global health challenge. Considerable successes have been recorded in a bid to eliminate HBV transmission yet; the prevalence of these infectious diseases still outweighs total elimination. Several mathematical models by researchers have modeled the control of the spread of HBV using different parameters and arriving at different intervention measures, [6].

The mathematical modelling of infectious diseases is primarily aimed at studying the spread and duration of epidemics, understanding the scale of the disease challenge and the potential impact of interventions; predicting the spread of the disease, total number of infected persons, duration of the epidemic, as well as reproduction numbers and then, identify the most efficient technique for issuing a limited number of vaccines in a given population, [7]. Researchers like [8], proposed that the infectivity during the incubation period can be a second way of transmission prompting, [9], [10], to study the global behavior of the spread of HBV using an SEIR model with a constant vaccination rate and the dynamics of Hepatitis B via a Susceptible Exposed Infectious Recovered (SEIR) type epidemic model. Their study showed that the endemic equilibrium was globally asymptotically stable since the disease persisted in the population and reproductive number $R_0 > 1$. Researchers have continued to look into the scientific ways of mitigating or correcting the continued spread of the infectious disease, some of which are [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21].

Since studies have shown that Hepatitis B is characterized by multiple endemic solutions, a matter which may be of concern in developing control strategies, [22], was able to identify the possible causes of multiple endemic solutions in a Hepatitis B model and concluded that the dependence of the probability of carriage development $(q(\Lambda))$ on the force of infection (Λ) is the main reason for multiple endemicity; that is where a large proportion of infants that are not vaccinated (ω)). Subsequently, [23], looked into the SIR epidemic model with a changing population size leaving the immigration rate constant. The stability properties of the equilibrium points of the model were analyzed indicating that the disease-free equilibrium point was stable and the population survived and for a stable endemic equilibrium point, the number of infectives did not change, meaning the infected rate equals the recovery rate. Furthermore, working on an SEIRS model with a time delay on complex networks, [24], was able to determine R_0 and equilibriums of the model from the mean field theory. Time delay cannot change the basic reproductive number because it is dependent on the topology of the underlying networks by theoretical analyses, and can reduce the endemic level and weaken the epidemic spreading. [25], made a comparison of two viruses; Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV) infection as a public health problem worldwide and the study concluded that the prevalence of HBV infection is higher than that of HIV among blood donors.

Then, [26], analyzed a class of discrete vertical and horizontal disease models with constant vaccination and population size. The obtained values were input into the eigenvalue determined from the model equations and discussed the influence of the coefficient parameter on the eigenvalues. This prompted [27] and [28], to look into R_0 of an age structured SEIR epidemic model with latency in its infectivity derived by using theories of both differential and integral equations. It was observed that the disease-free equilibrium is locally and globally asymptotically stable if $R_0 < 1$ and just one endemic equilibrium exists, if $R_0 > 1$. From literature, researches had focused more on vertical transmission of HBV infections than latency, thereby creating a lacunar. Hence, this research considers the combined effects of latent and vertical transmission of HBV infections and their dynamics of treatments, and vaccination. The objective is to see if the combination of vaccination and treatment can be an effective intervention means in mitigating and possibly eradicating the HBV infection.

2 Problem Formulation

Consider a complex but realistic SLITR model which captures an additional treatment compartment. The governing SLITR model considers an individual's infection in the latent category and considers the flow of disease from the susceptible category to other categories based on the following assumptions, [29], [30],

i). Members of the population are the same (homogeneous population);
ii). Recruitment of individuals into the population is only through birth;
iii). Exiting out of the population is through both natural death and virus-related death only;

iv). Individuals who received vaccination may not necessarily achieve permanent immunity;
v). Infants born by carrier mothers proceed to either susceptible or latent class immediately;
vi). Treated carriers recover; and
vii). Induced death is only in the infectious class.

The mathematical model compartmentalized the total human population into; susceptible individuals $S(t)$, latent individuals $L(t)$, infectious individuals $I(t)$ and recovered patients $R(t)$. Where, $(1-z)(B(t)-\kappa B_c(t))$ is the rate of recruitment of population into susceptible group, α the transmission coefficient from susceptible group to latent class, β the transmission rate from latent class to infectious class, $\kappa B_c(t)$ the recruitment rate into the latent population, μ and μ_c are the natural death rate which occurs in all the five classes and the Hepatitis B Virus related death rates respectively in the model system. Similarly, $(1-z)$ is the proportion of birth without vaccination, z the vaccinated proportion, κ the proportion of birth vertically infected (children infected during birth), $(1-\kappa)$ the proportion of children not vertically infected, ν the rate that recovered individuals become susceptible again, π the rate at which individuals in latent class go for treatment, ω the rate at which individuals in infectious class go for treatment, and γ the rate at which those that receive treatment recover.

From the SLITR model in Figure 1 (Appendix), the nonlinear ordinary differential systems of equations become:

$$\frac{dS}{dt} = (1-z)\big(B(t)\kappa B_c(t)\big) + \nu R - (\mu+\alpha)S \quad (1)$$

$$\frac{dL}{dt} = \alpha s + \kappa B_c(t) - (\mu+\pi+\beta)L \quad (2)$$

$$\frac{dI}{dt} = \beta L - (\omega+\mu_c+\mu)I \quad (3)$$

$$\frac{dT}{dt} = \pi L + \omega I - (\gamma+\mu)T \quad (4)$$

$$\frac{dR}{dt} = z(B(t) - \kappa B_c(t) + \gamma T - (\mu+\nu)R \quad (5)$$

subject to the axioms:

$$N = S + L + I + T + R \quad (6)$$

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dR}{dt}. \quad (7)$$

2.1 Analysis of the Model

The nonlinear differential system, Eq. (1) to Eq. (5), for all $t\epsilon[0, t_0]$, $S(t)$, $L(t)$, $I(t)$, $T(t)$ and $R(t)$ will be positive in R_5^+ since, all the parameters used in the model are entirely positive. Placing a lower bound on the equations, gives:

$$\frac{dS}{dt} = (1-z)\big(B(t) - \kappa B_c(t)\big) + \nu R - (\mu+\alpha)S \geq -(\mu+\alpha)S \quad (8)$$

$$\frac{dL}{dt} = \alpha s + \kappa B_c(t) - (\mu+\pi+\beta)L \geq -(\mu+\pi+\beta)L \quad (9)$$

$$\frac{dI}{dt} = \beta L - (\omega+\mu_c+\mu)I \geq -(\omega+\mu c+\mu)I \quad (10)$$

$$\frac{dT}{dt} = \pi L + \omega I - (\gamma+\mu)T \geq -(\gamma+\mu)T \quad (11)$$

$$\frac{dR}{dt} = z\big(B(t) - \kappa B_c(t)\big) + \gamma T - (\mu+\nu)R \geq -(\mu+\nu)R. \quad (12)$$

By the method of separation of variables, Eq. (8) becomes:

$$\frac{dS}{dt} \geq -(\mu+\alpha)S$$

$$\frac{dS}{S} \geq -(\mu+\alpha)dt. \quad (13)$$

and integrating both sides of Eq. (13), gives:

$$\ln S(t) - \ln S(0) \geq -(\mu+\alpha)t$$

$$S(t) \geq S(0)e^{-(\mu+\alpha)t},$$

as $t \to \infty$ and $e^{-\infty} = 0$

$$S(t) \geq 0, \quad \forall \quad t \geq 0\,. \tag{14}$$

Applying the same methods and principles of Eqs. (8) and (13) to Eqs. (9) – (12), gives

$$L(t) \geq L(0)e^{-(\mu+\pi+\beta)t}$$

$$L(t) \geq 0, \quad \forall\, t \geq 0 \tag{15}$$

$$I(t) \geq I(0)e^{-(\omega+\mu c+\mu)t}$$

$$I(t) \geq 0, \quad \forall\, t \geq 0 \tag{16}$$

$$T(t) \geq T(0)e^{-(\gamma+\mu)t}$$

$$T(t) \geq 0, \quad \forall\, t \geq 0 \tag{17}$$

$$R(t) \geq R(0)e^{-(\mu+\nu)t}$$

$$R(t) \geq 0, \quad \forall\, t \geq 0\,. \tag{18}$$

From Eqs. (14) – (18), $S(t)$, $L(t)$, $I(t)$, $T(t)$ and $R(t)$ are positive in R_5^+ for all $t\epsilon[0, t_0]$.

***Lemma**: There exist an S_M, L_M, I_M, T_M, R_M such that $S(t)$, $L(t)$, $I(t)$, $T(t)$, $R(t)$,*

$\lim_{t\to\infty} Sup(S(t)) \leq S_M, \lim_{t\to\infty} Sup(L(t)) \leq L_M,$

$\lim_{t\to\infty} Sup(I(t)) \leq I_M, \quad \lim_{t\to\infty} Sup(T(t)) \leq T_M,$

$\lim_{t\to\infty} Sup(R(t)) \leq R_M$, *for all* $t \epsilon [0, t_0]$.

Proof:

The boundedness of the solution for all $t \epsilon [0, t_0]$, $S(t)$, $L(t)$, $I(t)$, $T(t)$, and $R(t)$ is proved. Since all the constants used in the system are positive, then

$$\begin{pmatrix} \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI}{dt} + \frac{dT}{dt} + \frac{dR}{dt} = \\ (1-z)B(t) - (\mu+\alpha)S - (\mu+\pi+\beta)L \\ -(\omega+\mu c+\mu)I - (\gamma+\mu)T - (\mu+\nu)R \end{pmatrix} \tag{19}$$

$$\begin{pmatrix} \frac{d(S+L+I+T+R)}{dt} \leq \\ (1-z)B(t) \\ -min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu), \\ (\gamma+\mu),(\mu+\nu) \end{bmatrix} \\ (S+L+I+T+R)t \end{pmatrix} \tag{20}$$

$$\leq \begin{pmatrix} \frac{(1-z)B(t)}{min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu),(\gamma+\mu),(\mu+\nu) \end{bmatrix}} \\ \cdot K_0 e^{-min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu),(\gamma+\mu),(\mu+\nu) \end{bmatrix} t} \end{pmatrix}. \tag{21}$$

Taking the limit of the supremum of both sides gives:

$$\begin{bmatrix} \lim_{t\to\infty} Sup(S+L+I+T+R)(t) \leq \\ \lim_{t\to\infty} Sup\begin{pmatrix} \frac{(1-z)B(t)}{min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu),(\gamma+\mu),(\mu+\nu) \end{bmatrix}} \\ +K_0 e^{-min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu),(\gamma+\mu),(\mu+\nu) \end{bmatrix} t} \end{pmatrix} \end{bmatrix}$$

$$\begin{bmatrix} S_M = L_M = I_M = T_M = R_M = \\ \frac{(1-z)B(t)}{min\begin{bmatrix} (\mu+\alpha),(\mu+\pi+\beta), \\ (\omega+\mu c+\mu),(\gamma+\mu),(\mu+\nu) \end{bmatrix}} \end{bmatrix}. \tag{22}$$

Because $(S+L+I+T+R)(t)$ is bounded, $S(t)$, $L(t)$, $I(t)$, $T(t)$, and $R(t)$ are all bounded since $(S(t), L(t), I(t), T(t), R(t)) \leq (S+L+I+T+R)(t)$.

Then, $S(t) \leq S_M$, $L(t) \leq L_M$, $I(t) \leq I_M$, $T(t) \leq T_M$ and $R(t) \leq R_M$ for all $t\epsilon[0, t_0]$.

2.1.1 Disease Free Equilibrium (DFE) Point

The point at which there is no infection within the population in study or the point in which the population is free of disease is called the Disease-

Free Equilibrium (DFE) point. Equating the Eqs. (1) – (4) to zero, gives:

$$E^0 = \left(\frac{B(t) - \kappa B_c(t)}{(\mu + \alpha)}, 0, 0, 0, 0 \right) \quad (23)$$

such that,

$$L^0 = I^0 = T^0 = R^0 = 0. \quad (24)$$

Using the next generation matrix method to calculate R_0, the basic reproduction number is given by $\rho(F_0 V_0^{-1})$ where, F_0 is the Jacobian of f_i at E^0, f_i is the rate of appearance of new infection in the compartment i, V_0 is the Jacobian of v_i at E^0, and v_i represents the rate at which individuals are transferred into and out of the compartment i.

The population infected with the disease is represented by the following;

$$\alpha s + \kappa B_c(t) - (\mu + \pi + \beta)L = 0 \quad (25)$$

$$\beta L - (\omega + \mu c + \mu)I = 0 \quad (26)$$

$$\pi L + \omega I - (\gamma + \mu)T = 0. \quad (27)$$

Taking $x = (L, I, T)$,

$$\frac{dx}{dt} = f_i - v_i$$

where, F_0 is equal to the Jacobian of f_i and

$$E^0 = \begin{bmatrix} \alpha s & \kappa B_c(t) & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}. \quad (28)$$

$$v_0^{-1} = \begin{bmatrix} \frac{1}{(\mu+\pi+\beta)} & 0 & 0 \\ \frac{\beta}{(\mu+\pi+\beta)(\omega+\mu_c+\mu)} & \frac{1}{(\omega+\mu_c+\mu)} & 0 \\ \frac{\beta\omega+\pi(\omega+\mu_c+\mu)}{(\mu+\pi+\beta)[(\Upsilon+\mu)(\omega+\mu_c+\mu)]} & \frac{\omega}{(\Upsilon+\mu)(\omega+\mu_c+\mu)} & \frac{1}{(\Upsilon+\mu)} \end{bmatrix}. \quad (29)$$

Multiplying Eq. (28) and Eq. (29), gives

$$F_0 V_0^{-1} = \begin{bmatrix} \alpha s & \kappa B_c(t) & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{(\mu+\pi+\beta)} & 0 & 0 \\ \frac{\beta}{(\mu+\pi+\beta)(\omega+\mu_c+\mu)} & \frac{1}{(\omega+\mu_c+\mu)} & 0 \\ \frac{\beta\omega+\pi(\omega+\mu_c+\mu)}{(\mu+\pi+\beta)[(\Upsilon+\mu)(\omega+\mu_c+\mu)]} & \frac{\omega}{(\Upsilon+\mu)(\omega+\mu_c+\mu)} & \frac{1}{(\Upsilon+\mu)} \end{bmatrix} \quad (30)$$

$$F_0 V_0^{-1} = \begin{bmatrix} \frac{\alpha S}{(\mu+\pi+\beta)} + \frac{\beta\kappa B_c(t)}{(\mu+\pi+\beta)(\omega+\mu_c+\mu)} & \frac{\kappa B_c(t)}{(\omega+\mu_c+\mu)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}. \quad (31)$$

The basic reproduction number R_0 is given by the spectral radius of the matrix $F_0 V_0^{-1}$, that is, the highest absolute value of eigenvalues

$$R_0 = \rho(F_0 V_0^{-1})$$

$$\left(R_0 = \frac{\alpha(B(t) - \kappa B_c(t))}{(\mu + \pi + \beta)} + \frac{\beta\kappa B_c(t)}{(\mu + \pi + \beta)(\omega + \mu_c + \mu)} \right). \quad (32)$$

2.1.2 Endemic Equilibrium (EE) Point

For this disease to continue in the population, all the compartments must not be zero that is, $E^*(S^*, L^*, I^*, T^*, R^*) \neq 0$. Thus,

$$\left(S^* = \frac{\beta\kappa B_c(t) + (\mu + \pi + \beta)}{\begin{matrix}(\kappa B_c(t)) - \kappa B_c(t) \\ [\mu(\mu + \pi + \beta) - (\mu + \pi) + \\ (\mu + \alpha)(\mu + \pi + \beta) - \beta\alpha]\end{matrix}} \right) \quad (33)$$

$$L^* = \frac{\alpha S^* + \kappa B_c(t)}{(\mu + \pi + \beta)} \quad (34)$$

$$\left(I^* = \frac{\begin{matrix}(1 - z) \\ (B(t) - \kappa B_c(t))(\mu + \pi + \beta) \\ + \nu R(\mu + \pi + \beta) \\ -[(\mu + \alpha)(\mu + \pi + \beta) + \beta\alpha]S^* \\ + \beta\kappa B_c(t)\end{matrix}}{(\omega + \mu c + \mu)(\mu + \pi + \beta)} \right) \quad (35)$$

$$T^* = \frac{\pi L^* + \omega I^*}{(\gamma + \mu)} \quad (36)$$

$$R^* = \frac{z(B(t) - \kappa B_c(t)) + \gamma T^*}{(\mu + \nu)} \quad (37)$$

where, E^* exists if and only if $R_0 > 1$.

2.1.3 Local Stability of the DFE Point

The local stability is calculated using the Jacobian of the model at E^0. It is achieved using the sign of the real parts of the eigenvalues of the corresponding Jacobian matrix.

Theorem: *The disease-free equilibrium of the system of ODEs is locally asymptotically stable if the reproduction number* $R_0 < 1$ *and unstable if* $R_0 > 1$.

Proof:

Taking the equations of the system (1) – (5), the Jacobian matrix becomes

$$J = \begin{bmatrix} -(\mu+\alpha)S^0 & 0 & 0 & 0 & vR \\ \alpha S^0 & -(\mu+\pi+\beta)L & 0 & 0 & 0 \\ 0 & \beta L & -(\omega+\mu c+\mu)I & 0 & 0 \\ 0 & \pi L & \omega I & -(\gamma+\mu)T & 0 \\ 0 & 0 & 0 & \gamma T & -(\mu+v)R \end{bmatrix} \quad (38)$$

And $\boldsymbol{J}(E^0)$ gives;

$$J = \begin{bmatrix} -(\mu+\alpha)S^0 & 0 & 0 & 0 & v \\ \alpha S^0 & -(\mu+\pi+\beta) & 0 & 0 & 0 \\ 0 & \beta & -(\omega+\mu c+\mu) & 0 & 0 \\ 0 & \pi & \omega I & -(\gamma+\mu) & 0 \\ 0 & 0 & 0 & \gamma & -(\mu+v) \end{bmatrix} \quad (39)$$

By inspection, the matrix above shows that $\lambda_1 = -(\mu+\pi+\beta)$, $\lambda_2 = -(\mu+\alpha)$, and $\lambda_3 = -(\omega+\mu c+\mu)$ are the eigenvalues while the other two remaining eigenvalues are obtained from the 2×2 matrix,

$$\begin{vmatrix} -(\gamma+\mu)-\lambda & 0 \\ \gamma & -(\mu+v)-\lambda \end{vmatrix} = 0.$$

Using Routh-Hurwitz criterion, the disease-free equilibrium point E^0 is locally asymptotic stable if $a_1 > 0$ and $a_1 a_0 > 0$. Thus, for $a_1 > 0$,

$$(\gamma+\mu)(\mu+v) > 0, \gamma\mu + v\gamma + \mu^2 + \mu v > 0,$$

$$\gamma\mu + v\gamma + \mu^2 > -\mu v. \quad (40)$$

Dividing through Eq. (40) by $-\mu v$, gives

$$-\left(\frac{\gamma\mu + v\gamma + \mu^2}{\mu v}\right) < 1 \quad (41)$$

since, $R_0 < 1$, implies the disease-free equilibrium point is asymptotically stable.

2.1.4 Global Stability of the DFE Point

Using Castillo-Chavez approach, Eqs (8) – (11) can then be expressed as

$$\frac{dX_1}{dt} = F(X_1, X_2),$$

$$\frac{dX_2}{dt} = G(X_1, X_2), G(X_1, 0) = 0.$$

Where, $X_1 \in \Re^2 = (S^0, R^0)$ is the number of non-infected individuals and $X_2 \in \Re^3 = (L, I, T)$ is the infected compartment. Defining the conditions for global stability of disease-free equilibrium as

i). $\frac{dX_1}{dt} = (X, 0)$, X^0 is asymptotically stable

ii). $G(X_1, X_2) = AX_2 - G(X_1, X_2)$, $G(X_1, X_2) \geq 0$ for $(X_1, X_2) \in \Omega$

where, A the M–matrix for its off–diagonal elements are positive in the area, and Γ where the model equations make epidemiological sense. If the above two conditions are satisfied by the model system, then the theorem stated below is true.

Theorem: *Provided that* $R_0 < 1$ *and the conditions* $i)$. *and* $ii)$. *are satisfied, the disease-free equilibrium point* $E^0 = (X_0, 0)$ *of Eqs. (8) – (11) is globally asymptotically stable.*

Proof:

The DFE is now denoted as $E^0(X_1^*, 0)$ where $X_1^* = (N^0, 0)$. Now, the first condition of global asymptotically stability (GAS) is

$$\frac{dX_1}{dt} = F(X_1, 0). \quad (42)$$

Solving the linear differential equation, gives:

$$\begin{pmatrix} R^0(t) = \dfrac{z(B(t) - \kappa B_c(t) + \gamma T^0}{k_2} \\ -\dfrac{zB(t) - \kappa B_c(t) + \gamma T^0}{k_2} e^{-k_2 t} \\ +R^0(0)e^{-k_2 t} \end{pmatrix}. \quad (43)$$

And the solution indicates that, $S^0(t) + R^0(t) \to N^0(t)$ as $t \to \infty$ regardless of the values of $S^0(t)$ and $R^0(t)$. Therefore, $X_1^* = (N^0(t), 0)$ is globally asymptotically stable.

By the second condition, $G(X_1, X_2) = AX_2 - G(X_1, X_2)$ where $X_2 = (L^0, I^0, T^0)$

$$G(X_1, X_2) = \begin{bmatrix} \alpha s + \kappa B_c(t) - (\mu + \pi + \beta) L \\ \beta L - (\omega + \mu c + \mu) I \\ \pi L + \omega I - (\gamma + \mu) T \end{bmatrix} \quad (44)$$

$$A = \begin{bmatrix} \alpha s + \kappa B_c(t) & 0 & 0 \\ \beta & -(\omega + \mu c + \mu) & 0 \\ \pi & \omega & -(\gamma + \mu) \end{bmatrix} \quad (45)$$

$$G(X_1, X_2) = \begin{bmatrix} \alpha S^0 + \kappa B_c(t) - (\mu + \pi + \beta) L^0 \\ \beta L^0 - (\omega + \mu_c + \mu) I^0 \\ \pi L^0 + \omega I^0 - (\gamma + \mu) T^0 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad (46)$$

$$AX_2 = \begin{bmatrix} -(\mu + \pi + \beta) & 0 & 0 \\ \beta & -(\omega + \mu c + \mu) & 0 \\ \pi & \omega & -(\gamma + \mu) \end{bmatrix} \begin{bmatrix} L^0 \\ I^0 \\ T^0 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad (47)$$

$$G(X_1, X_2) = \begin{bmatrix} -(\mu + \pi + \beta) & 0 & 0 \\ \beta & -(\omega + \mu c + \mu) & 0 \\ \pi & \omega & -(\gamma + \mu) \end{bmatrix} \begin{bmatrix} L^0 \\ I^0 \\ T^0 \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad (48)$$

$G(X_1, X_2) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}^T$, $G(0,0) = 0$. Hence the proof is complete and the disease-free equilibrium is asymptotically stable, [31].

3 Numerical Solutions

This paper focuses on the possibility of eliminating infectious HBV by changing the data values assigned to vaccination and treatment. To obtain the numerical solution to Eqs. (1) to (5), MatLab is employed to simulate the systems and investigate the impact of both vaccination and treatment as a control strategy against infectious HBV on Latent and Infectious individuals. Some of the parameters for analysis were assumed based on the already established assumptions and also the fact that vaccination and treatment are combined, [32], [33], [34], [35], [36], as shown in Table 1 (Appendix).

The parameter values used are sufficiently small so that the analysis outputs remain relatively accurate when smaller parameter values are used. The assumptions made about the population do not and are not meant, in any way, to influence the simulation results but rather intended to optimize the analysis execution. Figure 2 (Appendix) shows the presence of the Hepatitis B Virus in the carrier population with vaccination intervention but no treatment administered to the infectious class. At the initial point where there are no both vaccinations and treatment $z = 0$, $\pi = 0$ and $\omega = 0$. The disease rises to the peak and decreases slightly and then remains almost stable all through the populations. The peak represents the epidemic crisis while the "almost stable state" indicates how the entire population is diseased. However, vaccination and treatment parameters of the Latent class at varying rates help alter the almost stable state of the pandemic and reduce it as shown by the green, blue, and yellow graphs.

Figure 3 (Appendix) indicates that without any intervention strategy, $z = 0$, $\pi = 0$ and $\omega = 0$, the population of the infectious class remains high, almost constant. However, when relatively high vaccinations and treatment efforts are made at the same rate of $z = 0.6$, $\pi = 0.6$, and $\omega = 0.6$, the disease persistence drastically reduces as shown by the blue graph among the infected. Interestingly, treating the infectious tends to be more effective than vaccinating them at the same rate as shown by the graphs of $z = 0$, $\pi = 0$, $\omega = 0.6$ compared to that of $z = 0.6$, $\pi = 0.6$, $\omega = 0$. This is because of relapse and resistance of infection to antibodies of the immune system.

Figure 4 (Appendix) shows that treating and vaccinating the carriers at the same rate will cause the disease to decrease but eradication is possible when the efforts are increased. This is attested to by the graph of $z = 0.9$, $\pi = 0.9$, and $\omega = 0.9$ in which intervention strategies are very high (Table 2, Appendix). Figure 5 (Appendix) shows infected population proportions in which only vaccination is administered and no treatment. The natural immune system fights the disease up to a relatively stable state. However increasing vaccination helps

supplement the immune system in the fight and reduction of the prevalence of disease among latent individuals. Figure 6 (Appendix) reveals that by combining both treatment and vaccination, the disease will be fully fought out of the population. The graph also indicates that for us to effectively bring full control over the infectious HBV disease, we have to increase the rate of implementing the two strategies.

Normalized Sensitivity Index

In this paper, the normalized sensitivity index is employed to measure and determine the best control measures using the reproduction number of the HBV model. Thus, quantify the developed model sensitivity by calculating changes in the reproduction number input parameters. Normalizing and comparing the sensitivity of each parameter in the model, makes it easy to assess the impact of various parameter input factors. Therefore, in the quest for best disease control measures, we identify and determine the most influential factor affecting the reproduction number output using the normalized sensitivity index denoted by $\Upsilon_{\beta}^{R_0}$ and defined by

$$\Upsilon_{\beta}^{R_0} = \frac{\beta}{R_0}\frac{\partial R_0}{\partial \beta}$$

with

$$\frac{\partial R_0}{\partial \beta} = -0.0104\,; \quad \text{and} \quad \frac{\beta}{R_0} = \frac{0.885}{0.017} \approx 52.2\,.$$

The relative change measure of R_0 with respect to β is,

$$\Upsilon_{\beta}^{R_0} = \frac{\beta}{R_0}\frac{\partial R_0}{\partial \beta} = 52.2(-0.0104) \approx -0.54\,.$$

Similarly, substituting the above numerical values, gives the normalized sensitivity index of the reproduction numbers as;

$$\Upsilon_{\mu}^{R_0} = \frac{\mu}{R_0}\frac{\partial R_0}{\partial \mu} \approx -0.0085\,;$$

$$\Upsilon_{\mu_c}^{R_0} = \frac{\mu_c}{R_0}\frac{\partial R_0}{\partial \mu_c} \approx -0.0028\,;$$

$$\Upsilon_{\kappa}^{R_0} = \frac{\kappa}{R_0}\frac{\partial R_0}{\partial \kappa} \approx -0.0299\,;$$

$$\Upsilon_{\alpha}^{R_0} = \frac{\alpha}{R_0}\frac{\partial R_0}{\partial \alpha} \approx 0.972\,;$$

$$\Upsilon_{B_c}^{R_0} = \frac{B_c}{R_0}\frac{\partial R_0}{\partial B_c} \approx -0.058\,;$$

$$\Upsilon_{\pi}^{R_0} = \frac{\pi}{R_0}\frac{\partial R_0}{\partial \pi} \approx -0.471\,;$$

$$\Upsilon_{\omega}^{R_0} = \frac{\omega}{R_0}\frac{\partial R_0}{\partial \omega} \approx -0.045\,;$$

$$\Upsilon_{B}^{R_0} = \frac{B}{R_0}\frac{\partial R_0}{\partial B} \approx 1\,.$$

Arranging the magnitude of the sensitivity analysis in descending order, determines the most sensitive parameter, that is,

$$B = 1, \alpha = 0.972, \beta = -0.54, \quad \pi = -0.471,$$

$$B_c = -0.058, \quad \omega = -0.045, \quad \kappa = -0.0299,$$

$$\mu = -0.0085, \mu_c = -0.0028.$$

Similarly, increasing the parameter values of $\beta = -0.54$, $\pi = -0.471$, $B_c = -0.058$, $\omega = -0.045$, $\kappa = -0.0299$, $\mu = -0.0085$, $\mu_c = -0.0028$ and reducing the value of the parameter values of B and α, will reduce the reproduction number and significantly reduce the spread of HBV. Figure 7 (Appendix) shows the bar chart MATLAB plot for the normalized sensitivity index analysis of each parameter in the reproduction number and π which represents rate at which individuals in latent class go for treatment was considered and increased by 0.3 in Figure 7(a), Figure 7(b) and Figure 7(c) in Appendix. Result shows that all other parameters in the reproduction number were affected by a slight increase in π, which implies that as more individuals yield

themselves for treatment, there is a corresponding decrease in β the transmission rate from the latent class of HBV disease, which suggests the disease awareness campaign (DAC).

4 Conclusion

A mathematical study of an infectious Hepatitis B Virus in which treatment and vaccination were combined in an attempt to predict the total eradication of the disease from the susceptible population was carried out. In this study, the existence, uniqueness, and boundedness of the solution were looked into as well as computing for the disease-free equilibrium point, basic reproduction number associated with the system, and endemic equilibrium point. To obtain the numerical result for the study, the Runge-Kutta fourth order scheme was used and implemented using MatLab. The obtained result showed that:

1. Vaccination and treatment can be effective intervention efforts to mitigate and possibly eradicate the prevalence of infectious HBV when administered at a higher rate.
2. A periodic mass vaccination of expecting mothers and children should always be carried out as this can set the basis for eliminating the hepatitis B Virus as shown in Figure 2 (Appendix).
3. Test and increase the level of treatment among latent individuals (Figure 5, Appendix).
4. In pursuit of total eradication of the Hepatitis B Virus pandemic, governments should double vaccination coupled with treatment programs among the susceptible populations (Figure 6, Appendix).
5. Continued educating of the nomad communities which are tightly held to unhealthy cultures like traditional methods of circumcision. This will help in eliminating unnecessary transmission of HBV which is usually contracted as a result of using non-sterilized objects for tattooing and circumcision.

For further research, a look into exploring the application of computational and artificial intelligence in resolving the complexity of the problems, would add value and enhance scientific output.

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References:

[1] Gasim, R.A., Eltayeb, N., Khidir, I., Hepatitis B Virus infection in pregnant women, in Al Fashir town, North Darfur State, Sudan, *Open Journal of Medical Microbiology*, Vol. 9, No. 1, 2019, pp. 28-36, https://doi.org/10.4236/ojmm.2019.91004.

[2] Huang, C., Fang, Y., Maternal blood milk saliva sample selection and the transmission of Hepatitis B Virus infectious research, *Open Journal of Obstetrics and Gynecology*, Vol. 9, No. 3, 2019, pp. 363-370, https://doi.org/10.4236/ojog.2019.93037.

[3] Viral Hepatitis B and C, European Commission, [Online]. https://health.ec.europa.eu/health-security-and-infectious-diseases/hivaids-hepatitis-and-tuberculosis/viral-hepatitis-b-and-c_en (Accessed Date: March 29, 2024).

[4] World Health Organization, *Global health strategy on viral hepatitis 2016-2021 towards ending viral hepatitis*, WHA69/2016/REC/1, June 2016, [Online]. https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06eng.pdf?sequence=1 (Accessed Date: March 29, 2024).

[5] Federal Ministry of Health, Abuja, Nigeria, *National guidelines for the prevention, care and treatment of viral hepatitis B and C in Nigeria*, National AIDS/STIS Control Program, 2016, [Online]. https://www.hepb.org/assets/Uploads/Nigeria-Hepatitis-Guidelines-TX-guidelines.pdf (Accessed Date: March 29, 2024).

[6] CDC Global Immunization, [Online]. https://www.cdc.gov/globalhealth/immunization/diseases/hepatitis-b/data/fast-facts.html (Accessed Date: March 29, 2024).

[7] Olajide, A.J., Afeez, A., Oluwaseun, J.O., Akinpelu, F.O., Mathematical modeling of transmission dynamics and optimal control of isolation, vaccination and treatment for Hepatitis B Virus, *General Letters in Mathematics*, Vol.5, No. 3, 2018, pp. 132-147, https://doi.org/10.31559/glm2018.5.3.3.

[8] Moneim, I.A., Mosa, G., Modelling childhood infectious diseases with infectious latent and loss of immunity, *Global Journal of Pure and Applied Mathematics*, Vol.16, No. 3, 2020, pp. 403-417.

[9] Moneim I.A., Khalil, H., Modelling and simulation of the spread of HBV disease with infectious latent, *Applied Mathematics*, Vol.6,

No. 5, 2015, pp. 745-753, https://doi.org/10.4236/am.2015.65070.

[10] Zhou, M., Zhang, T., Global analysis of an SEIR epidemic model with infectious force under intervention strategies, *Journal of Applied Mathematics and Physics*, Vol.7, No. 8, 2019, pp. 1706-1717, https://doi.org/10.4236/jamp.2019.781177.

[11] Onyango, N.O., Multiple endemic solutions in an epidemic Hepatitis B model without vertical transmission, *Applied Mathematics*, vol.5, No. 16, 2014, pp. 2518-2529, https://doi.org/10.4236/am.2014.516242.

[12] Thongchai, D., Tunwa, K., Rujira, O., Stability analysis of epidemic model with varying total population size and constant immigration rate, *Chiang Mai Journal of Science*, Vol.41, No. 2, 2014, pp. 470-485.

[13] Dong, J., Li, T., Wan, C., Liu, X.D., The analysis of a SEIRS epidemic model with time delay on complex networks, *Open Access Library Journal*, Vol.4, 2017, e3901, https://doi.org/10.4236/oalib.1103901.

[14] Police, S.M.C., Bessanguem, B., Mofini, E., Elowa, B., Service, G., Guerendo, P., Kalebanga, A.T.Y., Boua-Akelelo, N.P., Odilon, T.S.F., Kobendo, J.R.M., High Prevalence of Hepatitis B Virus Infection Compared to Human Immunodeficiency Virus among Blood Donors in Bangui, *Open Journal of Gastroenterology*, Vol.10, No. 6, 2020, pp. 137-143, https://doi.org/10.4236/ojgas.2020.106014.

[15] Li, M.S., Liu, X.M., Zhou, X.L., The dynamic behavior of a discrete vertical and horizontal transmitted disease model under constant vaccination, *International Journal of Modern Nonlinear Theory and Application*, Vol.5, No. 4, 2016, pp. 171-184, https://doi.org/10.4236/ijmnta.2016.54017.

[16] Xue-Zhi, L., Bin, F., Stability of an Age-structured SEIR Epidemic Model with Infectivity in Latent Period, *Applications and Applied Mathematics: An International Journal*, Vol.4, No. 1, 2019, pp. 218-236

[17] Lamin, B.C., Ousman, B.P., Sembene, P.M., Ceesay M., Joof, E., Kebbeh, A., Gueye, M., Njie, E., Sannch, B., Qualitative detection of Proviral–DNA of HIV–1 in infants to determine the efficacy of antiretroviral therapy in the prevention of vertical transmission of HIV–1 in the Gambia, *World Journal of AIDS*, Vol.6, No. 4, 2016, pp. 169-177, https://doi.org/10.4236/wja.2016.64019.

[18] Gölgeli M., A mathematical model of Hepatitis B transmission in Turkey. *Communications Faculty of Science University of Ankara Series A1 Mathematics and Statistics*, Vol.68, No. 2, 2019, pp. 1586-1595, https://doi.org/10.31801/cfsuasmas.544126.

[19] Symon, C., Moatlhodi, K., Estomih, S.M., Mathematical analysis of drug resistance in vertical transmission of HIV/AIDS, *Open Journal of Epidemiology*, Vol.3, No. 3, 2013, pp. 139-148, https://doi.org/10.4236/ojepi.2013.33021.

[20] Liu, J., Zhang, T., Global stability for delay SIR epidemic model with vertical transmission, *Open Journal of Applied Sciences*, Vol.2, No. 4, 2012, pp. 1-4, https://doi.org/10.4236/ojapps.2012.24B001.

[21] Fung J., Ching-Lung L., Young J., Wong D.K., Yeun J., Seto W., Yeun M., Stability of hepatitis B surface antigen over time: implications for studies using stored sera, *Journal of Medical Virology*, Vol.83, No. 11, 2011, pp. 1900-1904, https://doi.org/10.1002/jmv.22171.

[22] *Gender, Youth and Social Inclusion Analysis, USAID Regional Health Integration to Enhance Service-North*, Lango Project, February 15, 2018 – February 14, 2023, [Online]. https://pdf.usaid.gov/pdf_docs/PA00TN7Q.pdf (Accessed Date: March 29, 2024).

[23] Ministry of Health and Family Welfare, *Operational Guidelines for Hepatitis B vaccine in the universal immunization programme*, Ministry of Health and Family Welfare, Government of India, 2009, [Online]. https://pdf.usaid.gov/pdf_docs/PA00JZDT.pdf (Accessed Date: March 29, 2024).

[24] Zou, G.Y., Assessment of risk by predicting counterfactuals, *Statistics in Medicine*, Vol.28, No. 30, 2009, pp. 3761-3781, https://doi.org/10.1002/sim.3751.

[25] Zou, S., Stramer, S.L., Notari, E.P., Kuhns, M.C., Fang, C.T., Dodd, R.Y., Current incidence and residual risk of hepatitis B infection among blood donors in the United States, *Transfusion*, Vol.49, No. 8, 2009, pp. 1609-1620, https://doi.org/10.1111/j.1537-2995.2009.02195.x.

[26] Fact Sheets, *Hepatitis B*, World Health Organization, 18 July 2023. Hepatitis B (who.int), [Online]. https://www.who.int/news-room/fact-

sheets/detail/hepatitis-b (Accessed Date: March 29, 2024).

[27] Nikolaos T. Pyrsopoulos, Hepatitis B, *Gastroenterology*, updated October 20, 2022, [Online]. https://emedicine.medscape.com/article/177632-reference (Accessed Date: March 29, 2024).

[28] Grace C.Y.L., Ngai-Sze W., Rity Y.K.W., Yee-Kit T., Vincent W.S.W., Chi-Chiu L., Henry L.Y.C., and Grace L.H.W., Antiviral therapy for Hepatitis B prevents liver injury in patients with tuberculosis and Hepatitis B coinfection, *Clinical Infectious Diseases*, Vol. 70, No. 4, 2020, pp. 660-666. https://doi.org/10.1093/cid/ciz241.

[29] Khakshour A., Noori A., Keramati V., and Ghafourian M.S., Controlling Hepatitis B virus infection using PID like neural network, *2019 27th Iranian Conference on Electrical Engineering (ICEE)*, Yazd Iran, 2019, pp. 1221-1227.

[30] Y. Yin, G.Z. Li, Y. Wang, Q. Zhang, M. Wang, and L. Zhang, Analysis of the characteristics of Hepatitis B in various regions of China from 2009 to 2011 and the analysis of TCM diagnosis and treatment plans, *2021 IEEE International Conference on Bioinformatics and Biomedicine (BIBM)*, Houston, TX, USA, 2021, pp. 3912-3918.

[31] George Obaido, Blessing Ogbuokiri, Theo G. Swart, Nimibofa Ayawei, Sydney Mambwe Kasongo, Kehinde Aruleba, Ibomoiye Domor Mienye, Idowu Aruleba, Williams Chukwu, Fadekemi Osaye, Oluwaseun F. Egbelowo, Simelane Simphiwe, and Ebenezer Esenogho, An interpretable machine leaning approach for Hepatitis B diagnosis, *Applied Sciences*, Vol.12, No. 21, 2022, 11127, https://doi.org/10.3390/app122111127.

[32] D. Singh, S. Verma and J. Singla, A Neuro-fuzzy based Medical Intelligent System for the Diagnosis of Hepatitis B, *2021 2nd International Conference on Computation, Automation and Knowledge Management (ICCAKM)*, Dubai, United Arab Emirates, 2021, pp. 107-111.

[33] Norhidayah Abu, Noremylia Mohd Bakhori, and Rafidah Hanim Shueb, Lateral flow assay for Hepatitis B detection: a review of current and new assays, *Micromachines*, Vol.14, No. 6, 2023, 1239, https://doi.org/10.3390/mi14061239.

[34] Mangowi I., Mirambo M.M., Kilonzo S.B., Mlewa M., Nyawale H., Majinge D., Hyera F., Jaka H., Mtemisika C., Michael F., and Mshana S.E., Hepatitis B virus infection, associated factors, knowledge and vaccination status among household contacts of hepatitis B index cases in Mwanza, Tanzania, *IJID Regions*, Vol. 10, 2024, pp. 168-173, https://doi.org/10.1016/j.ijregi.2023.12.007

[35] Bader S. Alotaibi, Hepatitis B virus infection, structure, genotypes, and epidemiology – a review, *Pharmacy Practice*, Vol.21, No. 3, 2023, pp. 1-9, https://doi.org/10.18549/PharmPract.2023.3.2856

[36] Wu C.H., Hung C.L., Lee T.Y., Wu C.Y., and Chu W.C.C., Fatty liver diagnosis using deep learning in ultrasound image, *2022 IEEE International Conference on Digital Health (ICDH)*, Barcelona, Spain, 2022, pp. 185-192.

Contribution of Individual Authors to the Creation of a Scientific Article (Ghostwriting Policy)

The authors equally contributed in the present research, at all stages from the formulation of the problem to the final findings and solution.

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Conflict of Interest

The authors have no conflicts of interest to declare.

APPENDIX

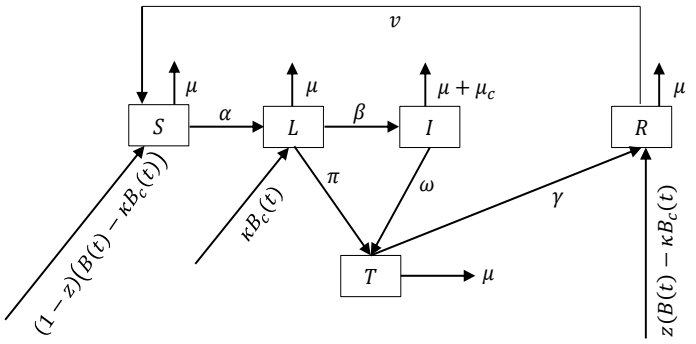


Fig. 1: Schematic diagram of the SLITR model for HBV

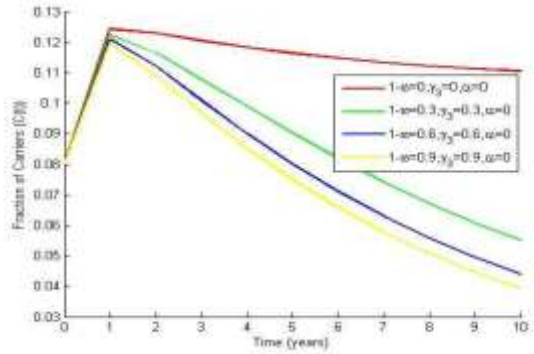


Fig. 2: Impacts of vaccination on Latent class without treatment

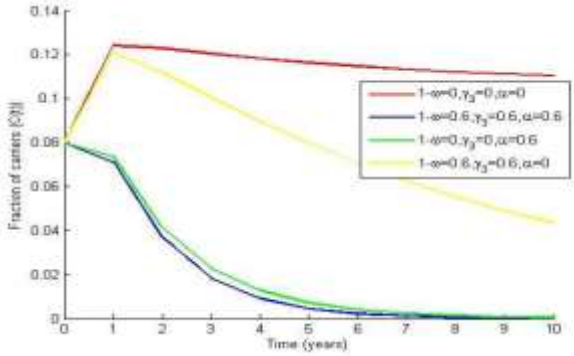


Fig. 3: Impact of low treatment and vaccination on the Latent class

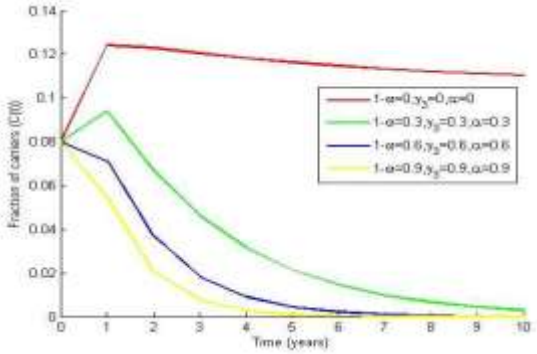


Fig. 4: Impact of equal rate of vaccination and treatment on Latent class

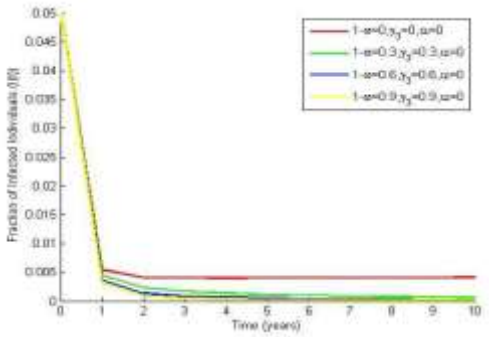


Fig. 5: Impact of increased treatment on Infectious individuals

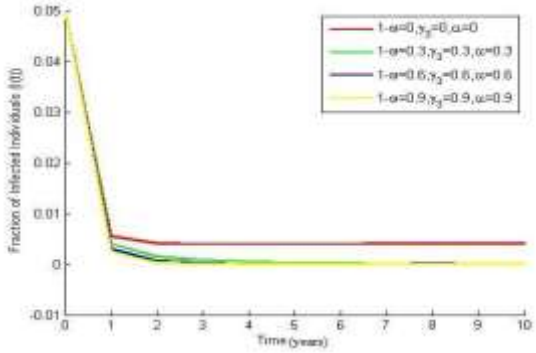
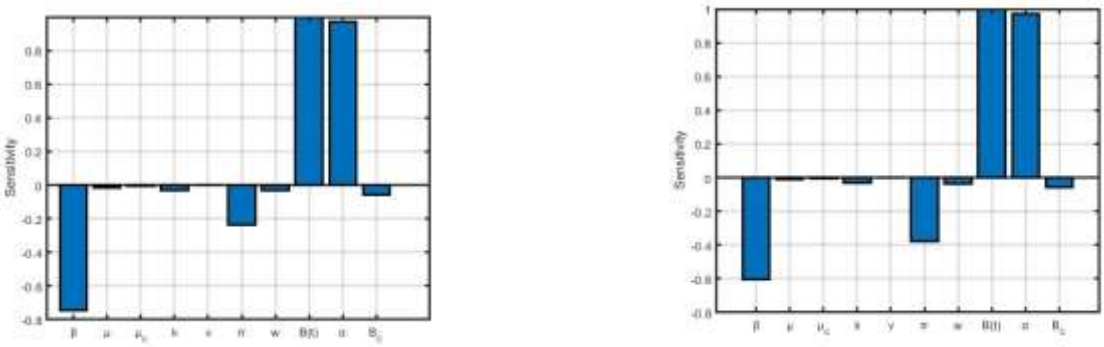
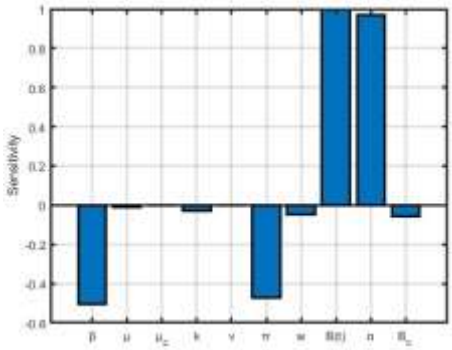


Fig. 6: Impact of both vaccination and treatment on Infectious individuals



(a) $\pi = 0.3$ (b) $\pi = 0.6$



(b) $\pi = 0.9$

Fig. 7: Bar chat of Normalized Sensitivity Index Analysis of HBV Reproduction number.

Table 1. Parameter for Numerical Simulation

Parameter	Value	References
$B(t)$	0.0367	[22], [23]
μ	0.0166	[22], [23]
μ_C	0.10	ASSUMED
$1-\mathrm{z}$	0.1	ASSUMED
κ	0.11	[24]
ν	0.1	[24], [25]
π	0.9	ASSUMED
γ	0.025	[24], [25]
z	0.9	ASSUMED
ω	0.9	ASSUMED
β	0.885	[25]
$B_c(t)$	0.0098	ASSUMED
α	0.9	ASSUMED

Table 2. Nomenclature of some Parameters

Parameter	Key
$1-\omega$	z (vaccinated children)
α	ω (Treatment parameter for infectious class)
γ_3	π (Treatment parameter for Latent class)