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MATHEMATICAL MODELLING OF THE TRANSMISSION DYNAMICS OF HEPATITIS B VIRUS IN THE PRESENCE OF IMPERFECT VACCINATION

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Abstract. Hepatitis B infection remains a global problem since the 1990s and the reasons for which disease is still in existence remain poorly understood. However, understanding the important role played by vaccination in the transmission dynamics of Hepatitis B virus is critical to its control and management. In this paper, an epidemiological model is proposed to model the spread of the Hepatitis B virus disease in the presence of imperfect vaccination. The basic reproduction number, $\mathbb{R}_0$ and the equilibria of the model are determined and the stabilities of the equilibria determined. It is shown that the disease-free equilibrium point is both locally and globally asymptotically stable when $\mathbb{R}_0 < 1$ while the endemic equilibrium point is proved to be locally asymptotically stable when $\mathbb{R}_0 > 1$. The model is also shown to exhibit a backward bifurcation phenomenon. Numerical simulations are carried out and it is observed that increasing both the vaccination and treatment rates reduces the populations of both the acutely infected and chronic carriers which eventually leads to the containment of the disease. We conclude that the combination of both vaccination and treatment with the use of a vaccine with a high efficacy is essential in the control of Hepatitis B virus disease.

Keywords: Hepatitis B virus (HBV); imperfect vaccination; treatment; simulations.
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1. INTRODUCTION

The revelations of the hepatitis B virus (HBV) infections started in the early 1966 [1]. Hepatitis B is a liver inflammation disease caused by the Hepatitis B virus (HBV). The virus is a global problem and the dangerous type among all the hepatitis viruses [3]. Hepatitis B virus (HBV) is a DNA virus with a circular genome formed by a partially double-stranded DNA, which reproduces through an RNA intermediate form by transcription which is very difficult to clear ones infected [4]. It infects the human hepatocytes in the liver as an acute or chronic infection and puts people at a high risk of death from cirrhosis of the liver and liver cancer. According to the World Health Organisation (WHO), more than 240 million people have long term liver infections and $780,000$ people die every year due to the acute or chronic consequences of the HBV infection [5]. Most of the infected individuals live in developing countries with few incidences in developed countries. In Ghana, HBV is a disease for individuals between the ages of 10 years to 50 years. About 1.6 million people in Ghana are chronic hepatitis B virus carriers [6]. Despite an effective vaccination program for newborn babies since the 1990s and treatment of infected patients, which has reduced chronic HBV infection in children [7, 8], the incidence of HBV infection is still on rise, from 21.9% in $100,000$ people in 1990 to 53.3% in $100,000$ in 2003 [9].

Mathematical modelling and numerical simulations are important tools that are useful in the control of human and animal infectious diseases. Over the years, vaccination of susceptible individuals with a hepatitis B vaccine and treatment of infected individuals with anti-viral therapies have proved to be partially efficient. It is of higher interest to understand the connections between the HBV, the human immune responses of the body, both the long-term and short-term effectiveness of the vaccine and drug efficacies and the overall well-being of the human liver. Mathematical models can be used to gain a clear understanding of disease transmission dynamics, assess the effectiveness of various prevention and control strategies. Several mathematical models of HBV transmission dynamics have focused on the influence of prevention and control measures that focused mainly on perfect vaccination, i.e when an individual is vaccinated, then they are fully protected from infection, antiviral treatment and linkage to care in certain regions

and countries.

In Zhang and Zhang [14], a mathematical model that incorporates perfect vaccination and treatment as control strategies to study the transmission dynamics of HBV in China is formulated. In Khan et al [11], a mathematical model to study the effect of immigrants on the host population with respect to HBV transmission is proposed. The model in [11] is a modification of the model in Pang, Cui and Zhou [12] that includes additional new transmission dynamics. These new transmission dynamics include; a migrated compartment, HBV transmission between the migrated compartment and the exposed compartment, the transmission between the migrated compartment and the acutely infected compartment and the natural death rate of individuals in the migrated compartment. The work presented in Zou, Zhang and Ruan [18] considers vertical transmission from carrier mothers to newborn babies in a bid to understand the transmission dynamics and control of HBV infection in mainland China. Kimbir et al [13], extend the work done in [18] to incorporate treatment as an HBV control measure. Moreover, Desta and Koya [15] classifies the infected population into chronic and acute compartments respectively and formulate a five compartment model to study the spread of HBV in Ethiopia. Both vaccination and treatment were incorporated as control strategies. The work in Zhang, Wang and Zhang [16], observed that incorporating both the exponential birth rate and vertical transmission in a mathematical model to study the transmission dynamics of HBV in Xinjiang, China proved beneficial. Hence, they proposed a model by incorporating vaccination of newborn babies and treatment as control strategies to study HBV.

The work done in Zhang and Zhou, [17], postulates that intrauterine infection in pregnant carrier mothers is relatively low, hence vertical transmission from HBV carriers mothers occurs either during delivery or after birth. They further claim that the acutely infected stage of HBV infection is relatively short compared to the pregnancy period of a carrier mother and the prolonged chronic phase of the HBV infection. Thus perinatal infection from carrier mothers who are acutely infected is not possible. These two characteristics of HBV transmission dynamics were used to formulate a mathematical model to describe the spread of hepatitis B virus disease in China. These mathematical models described above model the impact of perfect vaccination

and treatment as control strategies of HBV. HBV vaccines have been found not to protect those vaccinated fully. It is thus important to consider imperfect vaccination when modelling HBV infection. One of the feasible methods to predict the prevalence of any infectious disease is to use mathematical models [10]. In this paper, we extend the model in Zhang and Zhang [14] by taking into consideration imperfect vaccination in describing HBV transmission dynamics in the presence of treatment. We also incorporate vaccination at birth as in Zhang, Wang and Zhang [16]. We aim to investigate the transmission dynamics of HBV in the presence of an imperfect vaccine and vaccination at birth.

The paper is organized as follows; Section 2 is devoted to the mathematical formulation of the model. In Section 3 we present the model analysis, the basic reproduction number and the model equilibria. The stability analyses of the equilibria are given in 4. In Section 5, we study the numerical results of the proposed model and present the results and a discussion is presented in Subsection 5.7.

2. MODEL FORMULATION

Based on the fact that HBV vaccination is imperfect, we present a compartmental model of HBV transmission dynamics using an $SVICTR$ model with vaccination and treatment as intervention strategies with imperfect vaccination. We divide the total population at any time t, $N(t)$ into six compartments of: susceptible individuals $S(t)$, vaccinated individuals $V(t)$, acutely infected individuals $I(t)$, chronic carriers $C(t)$, treated individuals $T(t)$, immunized individuals $R(t)$, where

$$N(t) = S(t) + V(t) + I(t) + C(t) + T(t) + R(t).$$

The model is a system of ordinary differential equations with the assumption that recruitment into the susceptible population is driven by births and immigration at a rate λ and entire population is assumed to die at some natural death rate defined by μ_0. The virus is assumed to be horizontally transmitted at the rate of x, where x is defined as the force of infection, where

$$x = \beta(I + \eta_1 C + \eta_2 T)$$

with the parameters η_1 and η_2 measure the relative infectivity of individuals in compartments C and T respectively, when compared to those in compartment I. The parameter ω defines the proportion of individuals that are successfully immunized. The parameter θ denotes the rate at which individuals are vaccinated with the HBV vaccine while ψ is the rate at which the vaccine wanes. We further assume that vaccination with hepatitis B vaccine can reduce but not eliminate the susceptibility of infection. The results in a modified force of infection of the vaccinated defined by

$$z = \beta\,(1-\varepsilon)\,(I+\eta_1 C+\eta_2 T),$$

where $\varepsilon \in (0,1)$ is the efficacy of the vaccine. If $\varepsilon = 0$ then the vaccine is deemed to be useless while $\varepsilon = 1$ means the vaccines is 100% efficacious. Acutely infected individuals can either develop chronic HBV at a rate γ_1, recover at a rate $\bar{\omega}$, due to the immune response of the host. We assume that due to chronic infection, individuals may die as a result of the disease at an HBV-induced death rate μ_1. We also assume that both acutely and chronically infected individuals can undergo treatment at rates τ_1 and τ_2 respectively. Individuals under treatment can either recover at a rate σ or have treatment failure that results in them becoming chronically ill at a rate δ. The flow of individuals following the model description is shown in Figure 1.

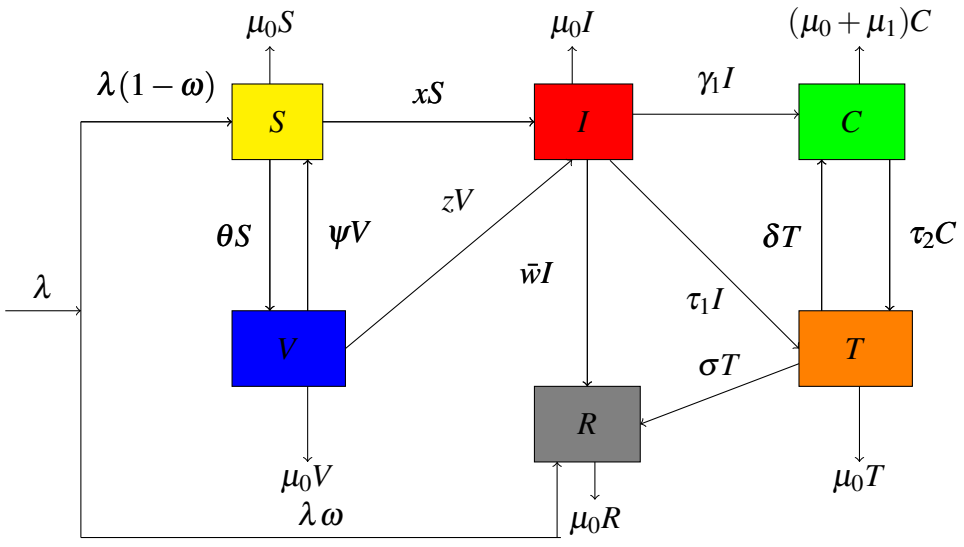

FIGURE 1. shows the schematic diagram of HBV transmission dynamics in the presence of an imperfect vaccination.

From the model diagram in Figure 1, we obtain a system of six ordinary differential equations that describe HBV transmission dynamics with treatment and imperfect vaccination. We have the following system of non-linear ordinary differential equations:

$$
\left.
\begin{aligned}
\frac{dS}{dt} &= \lambda(1-\omega) + \psi V - [\beta(I+\eta_1 C+\eta_2 T) + (\mu_0+\theta)]S,\\
\frac{dV}{dt} &= \theta S - [(\mu_0+\psi) + \beta(1-\varepsilon)(I+\eta_1 C+\eta_2 T)]V,\\
\frac{dI}{dt} &= \beta(I+\eta_1 C+\eta_2 T)S + \beta(1-\varepsilon)(I+\eta_1 C+\eta_2 T)V - (\mu_0+\gamma_1+\tau_1+\bar{\omega})I,\\
\frac{dC}{dt} &= \gamma_1 I + \delta T - (\mu_0+\mu_1+\tau_2)C,\\
\frac{dT}{dt} &= \tau_1 I + \tau_2 C - (\mu_0+\delta+\sigma)T,\\
\frac{dR}{dt} &= \lambda\omega + \bar{\omega} I + \sigma T - \mu_0 R.
\end{aligned}
\right\} \tag{1}
$$

Since the variable R does not appear in the other equations in system (1), the equation of R can be regards as redundant and the reduced system (2) can be studied.

$$
\left.
\begin{aligned}
\frac{dS}{dt} &= \lambda(1-\omega) + \psi V - [\beta(I+\eta_1 C+\eta_2 T) + (\mu_0+\theta)]S,\\
\frac{dV}{dt} &= \theta S - [(\mu_0+\psi) + \beta(1-\varepsilon)(I+\eta_1 C+\eta_2 T)]V,\\
\frac{dI}{dt} &= \beta(I+\eta_1 C+\eta_2 T)S + \beta(1-\varepsilon)(I+\eta_1 C+\eta_2 T)V - (\mu_0+\gamma_1+\tau_1+\bar{\omega})I,\\
\frac{dC}{dt} &= \gamma_1 I + \delta T - (\mu_0+\mu_1+\tau_2)C,\\
\frac{dT}{dt} &= \tau_1 I + \tau_2 C - (\mu_0+\delta+\sigma)T
\end{aligned}
\right\} \tag{2}
$$

3. Model Analysis

3.1. Positivity of Solutions. For system (2) to be biologically meaningful, we need to prove that all the state variables in the model system are non-negative. Thus, given any positive initial conditions, the solutions of system (2) should remain positive. We thus have the following lemma.

Lemma 1. Given that the initial solutions and parameters of system (2) are positive, the solutions $S(t)$, $V(t)$, $I(t)$, $C(t)$ and $T(t)$ are non-negative for all $t > 0$.

Proof. Let us consider

$$\kappa = \sup\{t > 0 : S(t) > 0, V(t) \geq 0, I(t) \geq 0, C(t) \geq 0, \quad \text{and} \quad T(t) \geq 0\}.$$

This implies that

$$S(t) > 0, \quad V(t) \geq 0, \quad I(t) \geq 0, \quad C(t) \geq 0$$
$$\text{and} \quad T(t) \geq 0, \quad \forall \quad t \in [0, \kappa).$$

Considering the first equation of system (2), we have

$$\frac{dS}{dt} = \lambda(1-\omega) + \psi V - [\beta(I + \eta_1 C + \eta_2 T) + (\theta + \mu_0)]S \quad \forall \quad t \in [0, \kappa).$$

Separating of variables and integrating, we obtain

$$S(\kappa) \geq S(0)\exp\left\{-(\theta+\mu_0)\kappa - \beta\left(\int_0^{\kappa}(I(t) + \eta_1 C(t) + \eta_2 T(t))dt\right)\right\} > 0.$$

For the second equation of system (2), we have

$$\begin{aligned}\frac{dV}{dt} &= \theta S - [(\mu_0 + \psi) + \beta(1-\varepsilon)(I + \eta_1 C + \eta_2 T)]V, \\ &\geq -[(\mu_0 + \psi) + \beta(1-\varepsilon)(I + \eta_1 C + \eta_2 T)]V.\end{aligned}$$

We similarly obtain

$$V(\kappa) \geq V(0)\exp\left\{-(\mu_0+\psi)\kappa - \beta(1-\varepsilon)\left(\int_0^{\kappa}(I(t) + \eta_1 C(t) + \eta_2 T(t))dt\right)\right\} \geq 0.$$

For the third equation of system (2), we have

$$I(\kappa) \geq I(0)\exp[-(\gamma_1 + \tau_1 + \mu_0 + \bar{\omega})\kappa] \geq 0.$$

Similarly, the remaining equations give the following

$$C(\kappa) \geq C(0)\exp[-(\mu_0 + \mu_1 + \tau_2)\kappa] \geq 0,$$

and

$$T(\kappa) \geq T(0)\exp[-(\delta + \sigma + \mu_0)\kappa] \geq 0.$$

Thus, the solutions $S(t) > 0, V(t) \geq 0, I(t) \geq 0, C(t) \geq 0$ and $T(t) \geq 0$ for all $t > 0$ given that:

$$S(0) > 0, \quad V(0) \geq 0 \quad I(0) \geq 0, \quad C(0) \geq 0, \quad \text{and} \quad T(0) \geq 0.$$

□

3.2. Boundedness of Solutions. Given the initial conditions of system (2) to be $S(0) > 0$, $V(0) \geq 0, I(0) \geq 0, C(0) \geq 0$ and $T(0) \geq 0$ and the fact that the model system we have monitors human population, it follows that the total population is given by

$$\bar{N}(t) = S(t)+V(t)+I(t)+C(t)+T(t),$$

with $\bar{N} \leq N$. The rate at which the total population is changing over time is given

$$\frac{d\bar{N}}{dt} = \lambda - \mu_0\bar{N} - \mu_1 C. \tag{3}$$

We have the following results on the boundedness of the model system in (2).

Lemma 2. The feasible region Ω is defined by the set:

$$\Omega = \left\{ (S(t),V(t),I(t),C(t),T(t)) \in {\mathbb{R}_+}^5 | \bar{N} \leq \frac{\lambda}{\mu_0} \right\}.$$

From (3), we have

$$\bar{N}(t) \leq \frac{\lambda}{\mu_0} + \left(N_0 - \frac{\lambda}{\mu_0} \right) e^{-\mu_0 t},$$

where $N_0 = \bar{N}(0)$. Hence, as $t \to \infty$, $N(t) \to \frac{\lambda}{\mu_0}$. So, if $N_0 < \frac{\lambda}{\mu_0}$, the total population at time t is bounded above by $\frac{\lambda}{\mu_0}$ and if $N_0 > \frac{\lambda}{\mu_0}$ the population decreases to $\frac{\lambda}{\mu_0}$. Therefore, for any solution $\{S(0) > 0, \quad V(0) \geq 0, \quad I(0) \geq 0, \quad C(0) \geq 0, \quad \text{and} \quad T(0) \geq 0\}$ at $t > 0$ of system (2) of the total population that begins in ${\mathbb{R}_+}^5$ either remains in or approaches Ω asymptotically. Hence, the region Ω is positively invariant and attracting with respect to system (2).

3.3. Disease-free Equilibrium (DFE). Equating the derivatives of system (2) to zero results in the disease-free equilibrium and the endemic equilibrium. At the disease-free equilibrium point there is no HBV in the population. Therefore, the disease-free equilibrium is given by

$$E_0(S^\star, V^\star, I^\star, C^\star, T^\star) = \left(\frac{\lambda(1-\omega)(\mu_0+\psi)}{\mu_0(\theta+\mu_0+\psi)}, \frac{\theta\lambda(1-\omega)}{\mu_0(\theta+\mu_0+\psi)}, 0, 0, 0 \right).$$

3.4. Basic Reproduction Number; $\mathbb{R}_0$. The basic reproduction number denoted by $\mathbb{R}_0$ is the average number of secondary HBV infections caused by an individual infected individual during his/her entire period of infectiousness. We use the next generation matrix operator as proposed by Diekmann and Heesterbeek [20] to compute the basic reproduction number. By the next generation matrix operator, the basic reproduction number is the spectral radius of the next-generation matrix denoted by $\rho(F_i V_i^{-1})$; where F_i is the rate at which secondary infections increase the infected compartments and V_i the rate at which infection progression and recovery decrease the infected compartment. It follows from system (2) that

$$F_i = \begin{pmatrix} \beta\,(I+\eta_1 C+\eta_2 T)\,S+\beta\,(1-\varepsilon)\,(I+\eta_1 C+\eta_2 T)\,V \\ 0 \\ 0 \end{pmatrix} \quad \text{and}$$

$$V_i = \begin{pmatrix} (\gamma_1+\tau_1+\mu_0+\bar{\omega})\,I \\ -\gamma_1 I-\delta T+(\mu_0+\mu_1+\tau_2)\,C \\ -\tau_1 I-\tau_2 C+(\delta+\sigma+\mu_0)\,T \end{pmatrix}.$$

The Jacobian of F_i and V_i at the DFE, we have

$$\mathbb{F}_i = \begin{pmatrix} \frac{\beta\lambda(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)]}{\mu_0(\theta+\mu_0+\psi)} & \frac{\beta\lambda\eta_1(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)]}{\mu_0(\theta+\mu_0+\psi)} & \frac{\beta\lambda\eta_2(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)]}{\mu_0(\theta+\mu_0+\psi)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$\mathbb{V}_i = \begin{pmatrix} \gamma_1+\tau_1+\mu_0+\bar{\omega} & 0 & 0 \\ -\gamma_1 & \mu_0+\mu_1+\tau_2 & -\delta \\ -\tau_1 & -\tau_2 & \delta+\sigma+\mu_0 \end{pmatrix}.$$

Hence the basic reproduction number is given by $\rho(\mathbb{F}_i \mathbb{V}_i)$ so that

$$\mathbb{R}_0 \;=\; \mathbb{R}_1+\mathbb{R}_2+\mathbb{R}_3,$$

where

$$\mathbb{R}_1 = \frac{\beta\lambda(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)]}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0+\bar{\omega})},$$

$$\mathbb{R}_2 = \frac{\beta\lambda\eta_1(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)](\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1)}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0+\bar{\omega})[(\mu_0+\mu_1+\tau_2)(\delta+\sigma+\mu_0)-\delta\tau_2]},$$

$$\mathbb{R}_3 = \frac{\beta\lambda\eta_2(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)](\gamma_1\tau_2+\tau_1(\mu_0+\mu_1+\tau_2))}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0+\bar{\omega})[(\mu_0+\mu_1+\tau_2)(\delta+\sigma+\mu_0)-\delta\tau_2]}.$$

The basic reproduction number, $\mathbb{R}_0$ is observed to be the sum of the reproduction number for the three infectious compartments. Thus $\mathbb{R}_1$ is the average number of secondary infections from the acutely infected compartment. Similarly, $\mathbb{R}_2$ is the average number of secondary infections from the chronically infected compartment whiles $\mathbb{R}_3$ represents that of the treatment compartment.

3.5. Endemic Equilibrium. The endemic equilibrium points are the steady-state solutions where the HBV persists in the population. Expressing the state variables in system (2) in terms of the variable C we obtain

$$\left.\begin{aligned} S^\star &= \phi_4 - \tfrac{(1-\varepsilon)\theta\phi_4}{\phi_5+\phi_6C^\star}, \\ V^\star &= \tfrac{\phi_7}{\phi_5+\phi_6C^\star}, \\ I^\star &= \phi_1C^\star, \\ T^\star &= \phi_2C^\star, \end{aligned}\right\} \tag{4}$$

where

$$\begin{aligned} \varepsilon_0 &= \lambda(1-\omega),\ \varepsilon_1=(\theta+\mu_0),\ \varepsilon_2=(\mu_0+\psi),\ \varepsilon_3=(\gamma_1+\tau_1+\mu_0+\bar{\omega}),\ \varepsilon_4=(\mu_0+\mu_1+\tau_2), \\ \varepsilon_5 &= (\delta+\sigma+\mu_0),\ \phi_1=\varepsilon_5\varepsilon_4\left[\frac{1-\Phi}{\gamma_1\varepsilon_5+\delta\tau_1}\right],\ \phi_2=\left[\frac{\gamma_1\tau_2+\tau_1\varepsilon_4}{\gamma_1\varepsilon_5+\delta\tau_1}\right],\ \phi_3=\phi_1+\eta_1+\eta_2\phi_2, \\ \phi_4 &= \frac{\varepsilon_3\phi_1}{\beta\phi_3},\ \phi_5=\theta(1-\varepsilon)+\varepsilon_2,\ \phi_6=\beta(1-\varepsilon)\phi_1+\beta(1-\varepsilon)\eta_1+\beta(1-\varepsilon)\eta_2\phi_2,\ \phi_7=\theta\phi_4, \\ \phi_8 &= \beta\phi_1+\beta\eta_1+\beta\eta_2\phi_2,\ \Phi=\frac{\delta\tau_2}{\varepsilon_5\varepsilon_4}<1, \end{aligned}$$

and

$$a_2(C^\star)^2+a_1C^\star+a_0 = 0. \tag{5}$$

The coefficients a_0, a_1 and a_2 are given by

$$\begin{aligned} a_2 &= \phi_8\phi_4\phi_6, \\ a_1 &= -\left[\varepsilon_0\phi_6 - \phi_8\phi_4\phi_5 + (1-\varepsilon)\,\phi_8\phi_7 - \varepsilon_1\phi_4\phi_6\right], \\ a_0 &= \varepsilon_1\phi_4\phi_5\left[1 - \frac{(\varepsilon_0\phi_5 + \varepsilon_1(1-\varepsilon)\,\phi_7)}{\varepsilon_1\phi_4\phi_5}\right] = \varepsilon_1\phi_4\phi_5(1-\mathbb{R}_0). \end{aligned}$$

From (5), we have

$$C^\star = \frac{-a_1 \pm \sqrt{a_1^2 - 4a_2a_0}}{2a_2}. \tag{6}$$

From (6), we have the following theorem:

Theorem 1. The model system in (2):

- has a unique endemic equilibrium point if $\mathbb{R}_0 > 1$;
- has two positive equilibria if $a_1 < 0$ for $\mathbb{R}_0 < 1$;
- otherwise has no positive endemic equilibrium.

4. Stability Analysis

In this section, we determine the global stability of the disease-free equilibrium.

4.1. Global Stability of Disease-free Equilibrium. We also apply the approach of Castillo-Chavez et al [19], to prove the global stability of the disease-free equilibrium. This approach is stated in the Theorem below.

Theorem 2. If a model system can be written in the form:

$$\begin{aligned} \frac{dX}{dt} &= F(X,I), \\ \frac{dI}{dt} &= G(X,I), \quad G(X,0) = 0, \end{aligned}$$

where $X \in \mathbb{R}^m$ denotes the number of uninfected individuals and $I \in \mathbb{R}^n$ denotes the number of infected individuals including latent, acute, infectious e.t.c. $U_0 = (X^\star, 0)$ denotes the disease-free equilibrium of the system. Then, the conditions (H_1) and (H_2) below must satisfied to guarantee local asymptotic stability.

(H_1) for $\frac{dX}{dt} = F(X^\star, 0)$, $X^\star$ is globally asymptotically stable.

(H_2) $G(X,I) = AI - \hat{G}(X,0) \geq 0$ for $(X,I) \in \Omega$, where $A = D_1 G(X^\star, 0)$ is a Metzler matrix (the off diagonal elements of A are non-negative) and Ω is the region where the model makes biological sense and well-posed. Then the fixed point $U_0 = (X^\star, 0)$ is globally asymptotically stable equilibrium of the hepatitis B virus model system (2) provided $\mathbb{R}_0 < 1$.

Theorem 3. The disease-free equilibrium of the model system $E_0 = (S^\star, V^\star, 0, 0, 0)$ is globally asymptotically stable if $\mathbb{R}_0 < 1$ and the conditions (H_1) and (H_2) are satisfied.

Proof. From system (2), $X \in \mathbb{R}^2 = (S,V)$ and $I \in \mathbb{R}^3 = (I,C,T)$. Hence for condition (H_1), we have

$$F(X,0) = \begin{pmatrix} \lambda(1-\omega) + \psi V - (\theta + \mu_0) S \\ \theta S - (\mu_0 + \psi) V \end{pmatrix}.$$

So, for the equilibrium $U_0 = (X^\star, 0)$, the system reduces to

$$\begin{aligned} \frac{dS(t)}{dt} &= \lambda(1-\omega) + \psi V - (\theta + \mu_0) S, \\ \frac{dV(t)}{dt} &= \theta S - (\mu_0 + \psi) V. \end{aligned}$$

It follows that

$$F(X,0) = \begin{pmatrix} -(\theta + \mu_0) & \psi \\ \theta & -(\mu_0 + \psi) \end{pmatrix}.$$

The characteristics polynomial of the system is given by

$$\alpha^2 + \alpha(2\mu_0 + \theta + \psi) + (\mu_0 + \theta)(\mu_0 + \psi)[1 - L] = 0, \tag{7}$$

where

$$L = \frac{\theta \psi}{(\mu_0 + \theta)(\mu_0 + \psi)} < 1.$$

Since all the coefficients of the characteristics polynomial in (7) are positive, by the Routh-Hurwitz criterion the solutions to the characteristic polynomial have negative real parts. This

means that the eigenvalues have negative real parts. Hence, $X^\star$ is always globally asymptotically stable. Also, applying Theorem 2 to the hepatitis B virus model system (2) gives

$$\begin{aligned} G(X,I) &= \begin{pmatrix} \Theta-(\gamma_1+\tau_1+\mu_0+\bar{\omega}) & \Theta\eta_1 & \Theta\eta_2 \\ \rho\gamma_1 & -(\mu_0+\mu_1+\tau_2) & \delta \\ \tau_1 & \tau_2 & -(\delta+\sigma+\mu_0) \end{pmatrix} \begin{pmatrix} I \\ C \\ T \end{pmatrix} \\ &\quad - \begin{pmatrix} \beta\left(I+\eta_1 C+\eta_2 T\right)\left(S^\star-S\right) \\ \beta\left(1-\omega\right)\left(I+\eta_1 C+\eta_2 T\right)\left(V^\star-V\right) \\ 0 \end{pmatrix}, \end{aligned}$$

where $\Theta=\beta S^\star+\beta\left(1-\omega\right)V^\star$. So, A is a Metzler matrix with non-negative off diagonal elements. Also, it follows from (3) that, as $t\to\infty$, $(I,C,T)\to(0,0,0)$. Therefore, $\hat{G}(X,I)\geq 0$ and the disease-free equilibrium is globally asymptotically stable. □

4.2. Bifurcation Analysis. System (2) give rise to multiple endemic equilibrium points which shows a bifurcation phenomenon at $\mathbb{R}_0=1$. We shall establish the conditions necessary and sufficient on the parameter values that cause the bifurcation phenomenon to system (1) based on the used of Centre Manifold Theory proposed by Castillo-Chavez and Song [21] and used in some published articles such as Opoku, Nyabadza and Gwasira [2] and Asamoah et al [25]. Choosing β as the bifurcation parameter and solving for $\beta=\beta^\star$ when $\mathbb{R}_0=1$, we obtain

$$\beta^\star = \frac{\mu_0\left(\theta+\mu_0+\psi\right)\left(\gamma_1+\tau_1+\mu_0+\bar{\omega}\right)\Psi_0}{\Psi_5\left[\Psi_0+\eta_1\left(\gamma_1\left(\delta+\sigma+\mu_0\right)+\delta\tau_1\right)+\eta_2\left(\gamma_1\tau_2+\tau_1\left(\mu_0+\mu_1+\tau_2\right)\right)\right]},$$

where $\Psi_0=\left(\mu_0+\delta+\sigma\right)\left(\mu_0+\mu_1+\tau_2\right)\left[1-\Upsilon\right]$, $\Upsilon=\dfrac{\delta\tau_2}{\left(\delta+\sigma+\mu_0\right)\left(\mu_0+\mu_1+\tau_2\right)}<1$,
$\Psi_5=\lambda\left(1-\omega\right)\left[\left(\mu_0+\psi\right)+\theta\left(1-\varepsilon\right)\right]$.

We redefine the state variables by letting $x_1=S(t)$, $x_2=V(t)$, $x_3=I(t)$, $x_4=C(t)$ and $x_5=T(t)$ so that the total host population $N(t)=S(t)+V(t)+I(t)+C(t)+T(t)$ becomes $N(t)=x_1+x_2+x_3+x_4+x_5$. Furthermore, by using vector notation, $\mathbf{x}=[S(t),V(t),I(t),C(t),T(t)]$, the system can be written in the form

$$\frac{d\mathbf{x}}{dt} = (f_1,f_2,f_3,f_4,f_5)$$

so that

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \lambda(1-\omega) + \psi x_2 - [\beta(x_3+\eta_1 x_4+\eta_2 x_5) + (\theta+\mu_0)]x_1,\\
\frac{dx_2}{dt} &= f_2 = \theta x_1 - [(\mu_0+\psi) + \beta(1-\varepsilon)(x_3+\eta_1 x_4+\eta_2 x_5)]x_2,\\
\frac{dx_3}{dt} &= f_3 = \beta(x_3+\eta_1 x_4+\eta_2 x_5)x_1 + \beta(1-\varepsilon)(x_3+\eta_1 x_4+\eta_2 x_5)x_2\\
&\quad -(\gamma_1+\tau_1+\mu_0+\bar{\omega})x_3,\\
\frac{dx_4}{dt} &= f_4 = \gamma_1 x_3 - (\mu_0+\mu_1+\tau_2)x_4 + \delta x_5,\\
\frac{dx_5}{dt} &= f_5 = \tau_1 x_3 + \tau_2 x_4 - (\delta+\sigma+\mu_0)x_5.
\end{aligned}$$

The Jacobian matrix evaluated at the disease-free equilibrium

$$E_0 = (S^\star, V^\star, 0, 0, 0) \quad \text{with} \quad \beta = \beta^\star \quad \text{is given as}$$

$$J_1 = \begin{pmatrix}
-\varepsilon_1 & \psi & -\beta^\star S^\star & -\beta^\star \eta_1 S^\star & -\beta^\star \eta_2 S^\star\\
\theta & -\varepsilon_2 & -w_3 & -w_4 & -w_5\\
0 & 0 & w_6 & w_7 & w_8\\
0 & 0 & \rho\gamma_1 & -\varepsilon_4 & \delta\\
0 & 0 & \tau_1 & \tau_2 & -\varepsilon_5
\end{pmatrix}.$$

The Jacobian matrix J_1 of the linearized system has a simple zero eigenvalue and all other eigenvalues have negative real parts. Hence, the Centre Manifold Theory can be used to analyse the stability dynamics of system (1). For the case when $\mathbb{R}_0 = 1$, we obtain the right eigenvector $q = (q_1, q_2, q_3, q_4, q_5)^T$ from the Jacobian matrix J_1 to be

$$\begin{aligned}
q_1 &= \left[\frac{\beta^\star\lambda(1-\omega)[\Psi_0+\Psi_1+\Psi_2+\Psi_3]}{\mu_0(\theta+\mu_0+\psi)[\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1]}\right],\\
q_2 &= \left[\frac{\beta^\star\lambda(1-\omega)[\Psi_0+\Psi_1+\Psi_2+\Psi_4]}{\mu_0(\theta+\mu_0+\psi)[\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1]}\right],\\
q_3 &= \left[\frac{\Psi_0}{\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1}\right],\\
q_4 &= 1,\\
q_5 &= \left[\frac{\gamma_1\tau_2+\tau_1(\mu_0+\mu_1+\tau_2)}{\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1}\right],
\end{aligned}$$

where $\Psi_1 = \eta_1(\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1)$, $\Psi_2 = \eta_2(\gamma_1\tau_2+\tau_1(\mu_0+\mu_1+\tau_2))$,
$\Psi_3 = \left[(\mu_0+\psi)^2+\left((\theta+\mu_0)(1-\varepsilon)+(\theta+\mu_0)^2(\mu_0+\psi)(1-\varepsilon)\right)\right]$,
$\Psi_4 = (\mu_0+\psi)+(\theta+\mu_0)(1-\varepsilon)$.

Also, we obtain the left eigenvector from the Jacobian matrix J_1 to be $v = (v_1, v_2, v_3, v_4, v_5)^T$ where

$$v_1 = 0,\ v_2 = 0,\ v_3 = 1,\ v_4 = \left[\frac{\beta^\star\Psi_5[\eta_1(\delta+\sigma+\mu_0)+\eta_2\tau_2]}{\mu_0(\theta+\mu_0+\psi)\Psi_0}\right],$$
$$v_5 = \left[\frac{\beta^\star\Psi_5[\delta\eta_1+\eta_2(\mu_0+\mu_1+\tau_2)]}{\mu_0(\theta+\mu_0+\psi)\Psi_0}\right].$$

From the transformed system, the associated non-zero partial derivatives of f evaluated at disease-free equilibrium which we need in the computation of a are given by

$$\frac{\partial^2 f_3(0,0)}{\partial x_1\partial x_3} = \frac{\partial^2 f_3(0,0)}{\partial x_3\partial x_1} = \beta^\star,\ \frac{\partial^2 f_1(0,0)}{\partial x_1\partial x_3} = \frac{\partial^2 f_1(0,0)}{\partial x_3\partial x_1} = -\beta^\star,$$

$$\frac{\partial^2 f_3(0,0)}{\partial x_1\partial x_4} = \frac{\partial^2 f_3(0,0)}{\partial x_4\partial x_1} = \beta^\star\eta_1,$$

$$\frac{\partial^2 f_1(0,0)}{\partial x_1\partial x_4} = \frac{\partial^2 f_1(0,0)}{\partial x_4\partial x_1} = -\beta^\star\eta_1,\ \frac{\partial^2 f_3(0,0)}{\partial x_1\partial x_5} = \frac{\partial^2 f_3(0,0)}{\partial x_5\partial x_1} = \beta^\star\eta_2,$$

$$\frac{\partial^2 f_1(0,0)}{\partial x_1\partial x_5} = \frac{\partial^2 f_1(0,0)}{\partial x_5\partial x_1} = -\beta^\star\eta_2,$$

$$\frac{\partial^2 f_3(0,0)}{\partial x_2\partial x_3} = \frac{\partial^2 f_3(0,0)}{\partial x_3\partial x_2} = \beta^\star(1-\varepsilon),\ \frac{\partial^2 f_3(0,0)}{\partial x_2\partial x_4} = \frac{\partial^2 f_3(0,0)}{\partial x_4\partial x_2} = \beta^\star\eta_1(1-\varepsilon),$$

$$\frac{\partial^2 f_3(0,0)}{\partial x_2\partial x_5} = \frac{\partial^2 f_3(0,0)}{\partial x_5\partial x_2} = \beta^\star\eta_2(1-\varepsilon),\ \frac{\partial^2 f_2(0,0)}{\partial x_2\partial x_3} = \frac{\partial^2 f_2(0,0)}{\partial x_3\partial x_2} = -\beta^\star(1-\varepsilon),$$

$$\frac{\partial^2 f_2(0,0)}{\partial x_2\partial x_4} = \frac{\partial^2 f_2(0,0)}{\partial x_4\partial x_2} = -\beta^\star\eta_1(1-\varepsilon),\ \frac{\partial^2 f_2(0,0)}{\partial x_2\partial x_5} = \frac{\partial^2 f_2(0,0)}{\partial x_5\partial x_2} = -\beta^\star\eta_2(1-\varepsilon)$$

and all the other second-order partial derivatives are equal to zero. Following [21], we have

$$a = v_3\sum_{i,j=1}^{5} q_i q_j \frac{\partial^2 f_3(0,0)}{\partial x_i\partial x_j}.$$

Hence,

$$\begin{aligned} a &= 2v_3\Big\{\beta^\star q_1q_3+\beta^\star\eta_1q_1q_4+\beta^\star\eta_2q_1q_5+\beta^\star(1-\varepsilon)q_2q_3 \\ &\quad +\beta^\star\eta_1(1-\varepsilon)q_2q_4+\beta^\star\eta_2(1-\varepsilon)q_2q_5\Big\}>0. \end{aligned}$$

Also, from the transformed system, the associated non-zero partial derivatives of f evaluated at the disease-free equilibrium which we need in the computation of b are given as

$$\frac{\partial^2 f_3}{\partial x_3\partial\beta}=\frac{\Psi_5}{\mu_0(\theta+\mu_0+\psi)},\ \frac{\partial^2 f_3}{\partial x_4\partial\beta}=\frac{\Psi_5\eta_1}{\mu_0(\theta+\mu_0+\psi)},\ \frac{\partial^2 f_3}{\partial x_5\partial\beta}=\frac{\Psi_5\eta_2}{\mu_0(\theta+\mu_0+\psi)}.$$

From

$$b = v_3\sum_{i=1}^{5}q_i\frac{\partial^2 f_3(0,0)}{\partial x_i\partial\beta},$$

we have

$$b = v_3\left[q_3\frac{\partial^2 f_3(0,0)}{\partial x_3\partial\beta}+q_4\frac{\partial^2 f_3(0,0)}{\partial x_4\partial\beta}+q_5\frac{\partial^2 f_3(0,0)}{\partial x_5\partial\beta}\right].$$

By substitution, we obtain

$$\begin{aligned} b &= \frac{\Psi_5\eta_1}{\mu_0(\theta+\mu_0+\psi)}+\frac{\Psi_5\Psi_0}{\mu_0[\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1](\theta+\mu_0+\psi)} \\ &\quad +\frac{\Psi_5\eta_2[\gamma_1\tau_2+\tau_1(\mu_0+\mu_1+\tau_2)]}{\mu_0[\gamma_1(\delta+\sigma+\mu_0)+\delta\tau_1](\theta+\mu_0+\psi)}>0. \end{aligned}$$

Since $a>0$ and $b>0$ holds when $\mathbb{R}_0=1$, system (2) undergoes a backward bifurcation at $\mathbb{R}_0=1$ and has a negative unstable endemic equilibrium point ($E^\star$) which becomes negative and locally asymptotically stable past $\mathbb{R}_0=1$.

We also use numerical simulations to show the stability and existence of the endemic equilibrium. Figure 2 below shows the bifurcation diagram of system (2). The chronically infected population at equilibrium plotted against the basic reproduction number $\mathbb{R}_0$ shows a backward bifurcation when $\mathbb{R}_0=1$, leading to the existence of multiple endemic equilibria. The lower dashed curve with a negative slope indicates unstable endemic equilibria and the upper bold curve with a positive slope indicates locally stable endemic equilibria. The diagram shows that when the basic reproduction number, $\mathbb{R}_0$ is less than one then eradication of the disease depends on the size of the population under consideration. However, reducing the value of $\mathbb{R}_0$ to

below $\mathbb{R}_0^\star$ called the $\mathbb{R}_0$ critical which is obtained by setting the discriminant of the quadratic polynomial in (6) to zero to gives

$$\mathbb{R}_0^\star = 1 - \left(\frac{a_1^2 + \phi_{10}}{4a_2\phi_9}\right),$$

where $\phi_9 = \dfrac{1}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0+\bar{\omega})\Psi_0}$, $\phi_{10} = \dfrac{\theta\psi}{\mu_0(\theta+\mu_0+\psi)}$, may result in controlling the HBV disease. This condition is guaranteed when the disease-free equilibrium state is globally asymptotically stable.

Thus, an increase in the vaccine efficacy to a value close to one $(i.e \quad \varepsilon \approx 1)$ will lead to the disappearance of the backward bifurcation curve. The biological meaning is that with an increase in the efficacy which corresponds with the extinction of the backward bifurcation curve, lowering $\mathbb{R}_0 < 1$ will be sufficient to eliminate the HBV disease from the population. Hence, $\mathbb{R}_0 < 1$ would be enough to make the disease-free equilibrium globally stable.

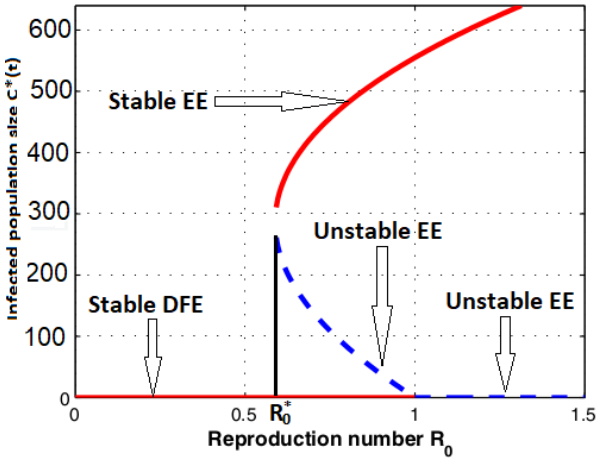

FIGURE 2. Backward bifurcation analysis of system (2) with the transmission rate β chosen as the bifurcation parameter. The saddle-node bifurcation occurs at $\mathbb{R}_0 = \mathbb{R}_0^\star$, where the stable endemic equilibrium state intersects the other unstable endemic equilibrium state.

5. NUMERICAL SIMULATIONS

In this section, we show the numerical simulations of the proposed model. We rely on values obtained from literature and estimated some of the parameter values for the spread of the HBV

disease. We conduct numerical simulations using Matlab. The initial conditions of the state variables are given to be $S(0) = 50000$, $V(0) = 40000$, $I(0) = 30000$, $C(0) = 20000$, $T(0) = 10000$ and the rest of the parameters and their values are presented in Table 1.

TABLE 1. Parameters and their values

Parameter	Standard value/year	Source	Parameter	Standard value/year	Source
λ	20000	Assumed	ω	0.65	[14]
μ_0	0.0166	[13]	$\bar{\omega}$	0.9	Assumed
μ_1	0.025	[15]	δ	0.2323	[14]
β	0.0017	Assumed	ψ	0.1	[22]
σ	$0.06 \leq \sigma \leq 0.6$	Assumed	η_1	0.4002	[14]
γ_1	0.1	Assumed	η_2	1.7352	[14]
τ_1	0.0576	[14]	θ	0.4	[15]
τ_2	0.0936	[14]	ε	$0 \leq \varepsilon \leq 1$	[23]

5.1. Numerical Results in the Presence of Perfect Vaccination. Figure 3 demonstrate how the reproduction number, $\mathbb{R}_0$ is evolve with a vaccination rate $\theta = 0.4$, treatment rate $\sigma = 0.6$ and a strong vaccine efficacy rate $\varepsilon = 1$. With other parameter values stated in Table 1, we observe that the model system settles at the disease-free state with $\mathbb{R}_0 = 0.9137$. However, due to constant recruitment of individuals into the susceptible population and the presence of individuals being vaccinated, the susceptible compartment shows a downward sloping curve that decreases and asymptotically approaches zero. This shows the effect perfect vaccination has on the number of susceptible individuals. The presence and application of vaccines causes the vaccinated individuals to increase while the infective compartments tend to zero since there is no transmission of the HBV in the population. Figure 3 has also confirmed the local and global

stability of the hepatitis B virus model at the disease-free equilibrium state. The biological meaning is that the hepatitis B virus disease will die out of the total population in the short-run period, say four years.

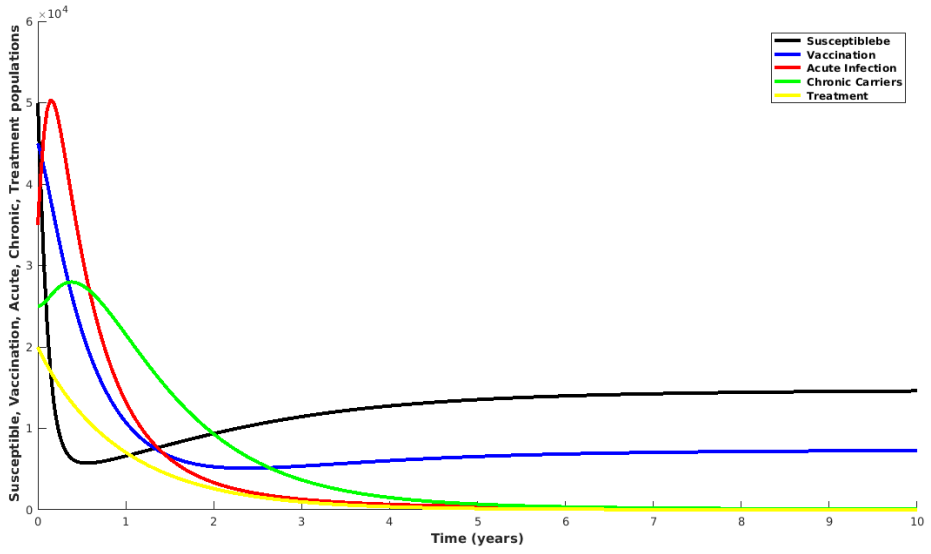

FIGURE 3. Numerical Simulation of $SVICTR$ Model for $\mathbb{R}_0 < 1$.

To further investigate the evolution of the reproduction number with the vaccination rate θ, treatment rate σ and vaccine efficacy rate, ε, we vary the values of these three parameters (θ, σ and ε). The results in Figure 4 below also shows that our model system 1 attained the endemic equilibrium state with the reproduction number, $\mathbb{R}_0 = 2.8124$ base on the parameter values in Table 1 above. The presence of the hepatitis B virus has increased the number of individuals in the infective compartments as depict in Figure 4 below.

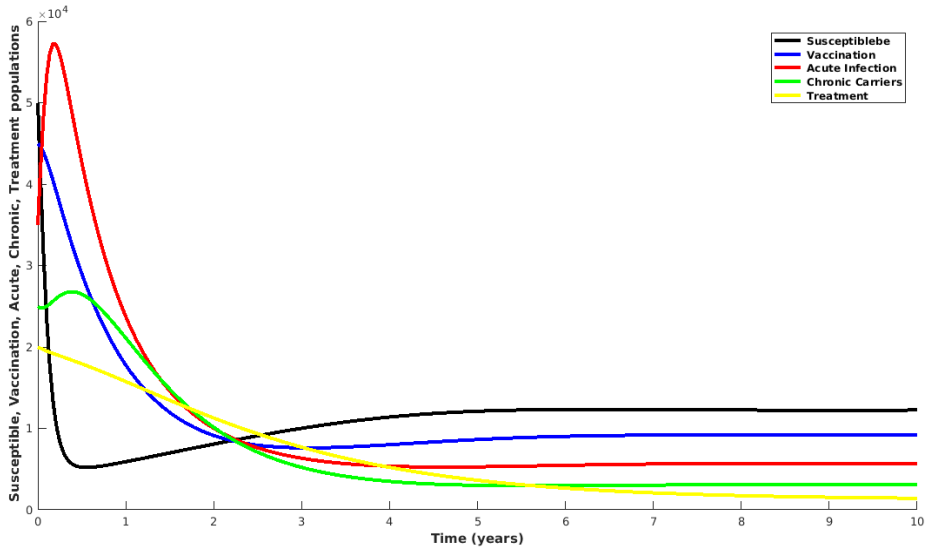

FIGURE 4. Numerical Simulation of $SVICTR$ Model for $\mathbb{R}_0 > 1$.

5.2. Effect of Perfect Vaccination on Acutely Infected and Chronic Carriers Population.

In Figures 5 and 6 below, we notice that as we increase the vaccination rate from 0.4 to 0.6 and 0.9 with a vaccine efficacy rate, say $\varepsilon = 1$, there is a corresponding decreased in both the acutely infected and chronic carriers populations. This implies that most of the individuals in the susceptible compartment have been vaccinated causing a reduction in the number of individuals who get infected with the hepatitis B virus disease. The simulation results in Figures 5 and 6 below demonstrate the important role perfect vaccination play in controlling the spread of hepatitis B virus disease in the population.

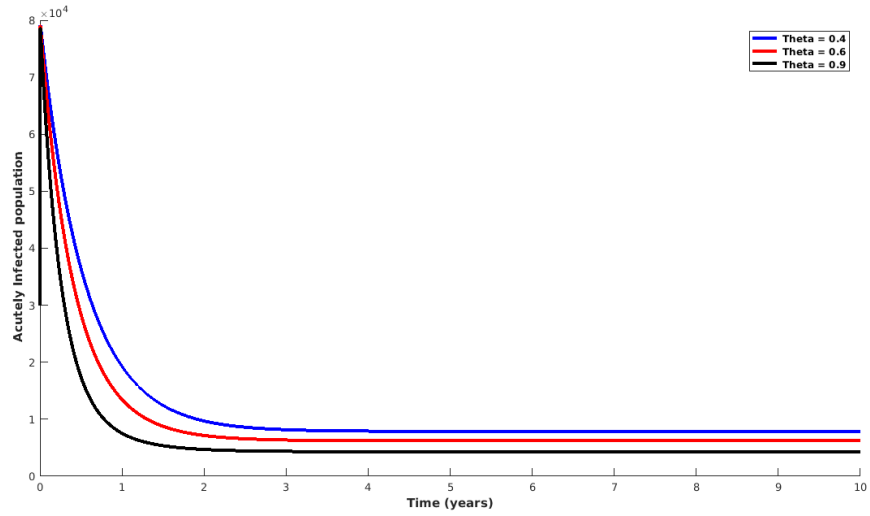

FIGURE 5. Simulation results showing the effect of varying the vaccination rate ($\theta = 0.4,\ \theta = 0.6,\ \theta = 0.9$) with vaccine efficacy rate, $\varepsilon = 1$ on the acutely infected population and the rest of the parameter values, as stated in Table 1.

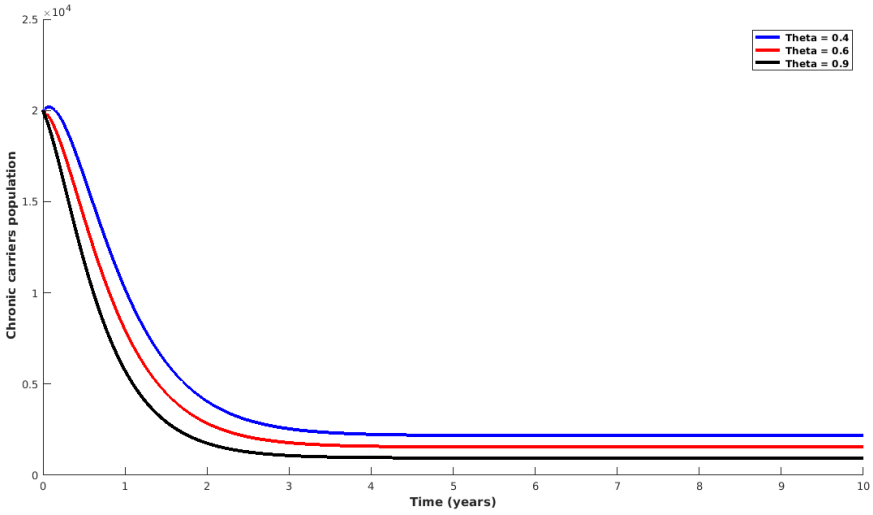

FIGURE 6. Simulation results showing the effect of varying the vaccination rate, ($\theta = 0.4,\ \theta = 0.6,\ \theta = 0.9$) with vaccine efficacy rate, $\varepsilon = 1$ on the chronic carriers population and the rest of the parameter values, as stated in Table 1.

5.3. Effect of Imperfect Vaccination on Acutely Infected and Chronic Carriers Population. In Figures 7 and 8 below, we notice that as we increased the vaccination rate from 0.4 to 0.6 and 0.9 with a weak vaccine efficacy rate, say $\varepsilon = 0.1$, there is a small corresponding decreased in both the acutely infected and chronic carriers populations. This implies that, though most of the individuals in the susceptible compartment have been vaccinated with the hepatitis B vaccine, only a small percentage of these individuals vaccinated are protected against the hepatitis B virus. Hence, the a small reduction in the number of individuals who get infected with hepatitis B virus disease. The simulation results in Figures 7 and 8 below demonstrate the important role imperfect vaccination play in preventing the spread of hepatitis B virus disease in the population.

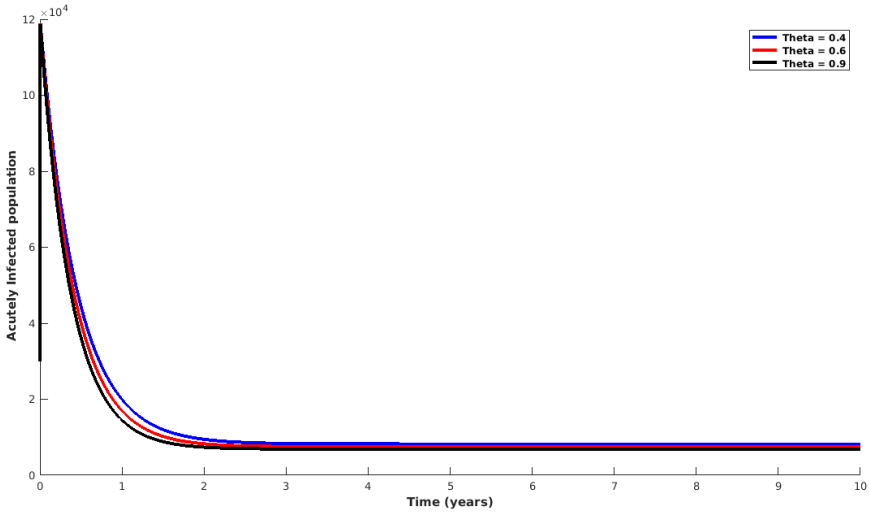

FIGURE 7. Simulation results showing the effect of varying the vaccination rate ($\theta = 0.4$, $\theta = 0.6$ and $\theta = 0.9$) with vaccine efficacy rate, $\varepsilon = 0.1$ on the acutely infected population and the rest of the parameter values, as stated in Table 1.

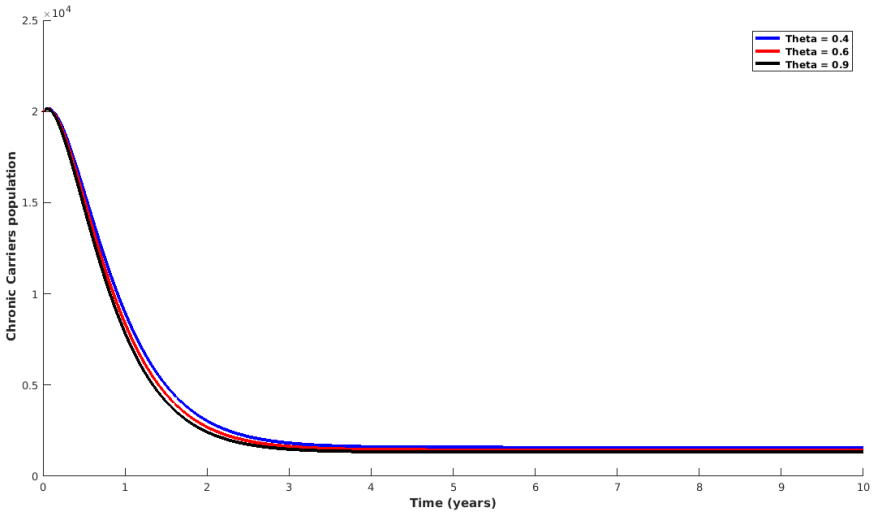

FIGURE 8. Simulation results showing the effect of varying the vaccination rate ($\theta = 0.4$, $\theta = 0.6$ and $\theta = 0.9$) with vaccine efficacy rate, $\varepsilon = 0.1$ on the chronic carriers population and the rest of the parameter values, as stated in Table 1.

5.4. Effect of Treatment on Acutely Infected and Chronic Carriers Population. We have observe in Figures 9 and 10 below that as the treatment rate, σ increases from $\sigma = 0.04$ to $\sigma = 0.06$ and $\sigma = 0.09$, there is a corresponding decreased in both acutely infected and chronic carriers population sizes respectively. This shows that the treatment of acutely infected and chronic carriers individuals has a great impact on eradicating the hepatitis B virus disease. Hence, the general public should be educated on the importance of seeking medical treatment when infected with the hepatitis B virus to help eliminate the disease.

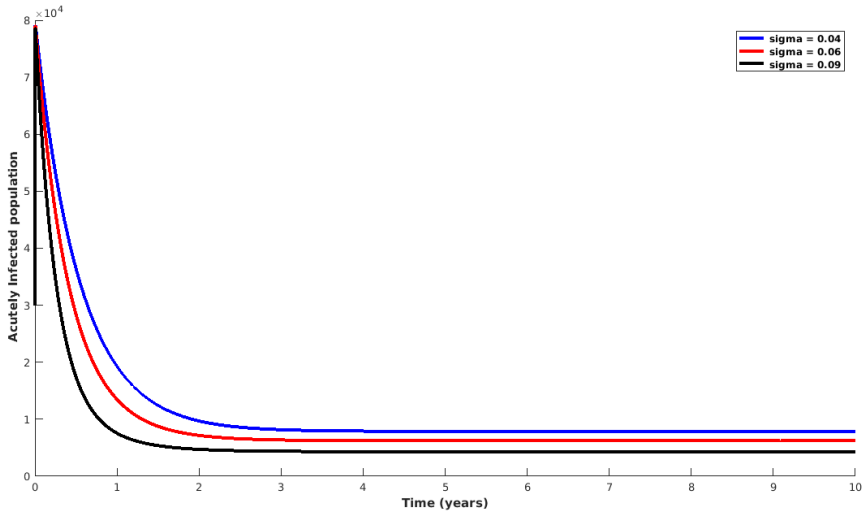

FIGURE 9. Simulation results showing the effect of varying the treatment rate ($\sigma = 0.04$, $\sigma = 0.06$, $\sigma = 0.09$) on the acutely infected population and the rest of the parameter values, as stated in Table 1.

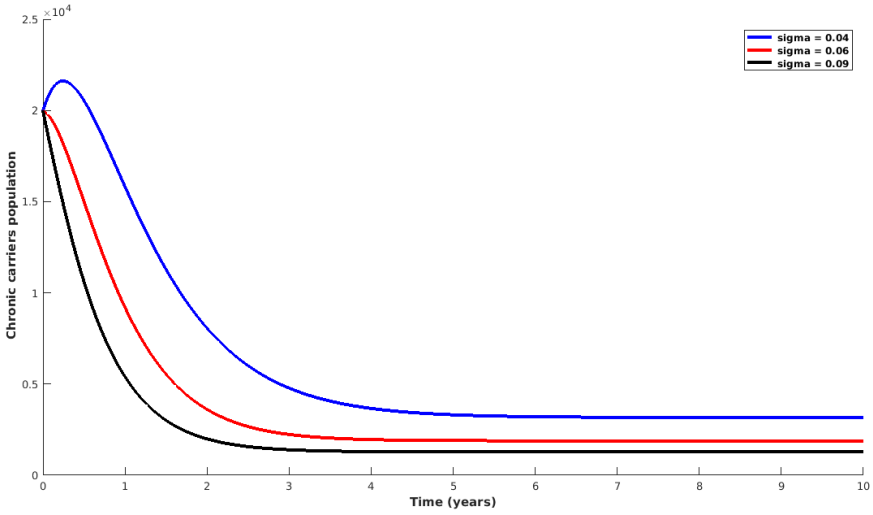

FIGURE 10. Simulation results showing the effect of varying the treatment rate ($\sigma = 0.04$ $\sigma = 0.06$, $\sigma = 0.09$) on the chronic carriers population and the rest of the parameter values, as stated in Table 1.

5.5. Effect of both Vaccination and Treatment on Acutely Infected and Chronic Carriers Population. Figures 11, 12, 13 and 14 below shows the effect of combining both treatment and vaccination with a high vaccine efficacy rate as control strategies of HBV infection. The main aim was to determine the best control strategy. Figure 11 shows the prevalence of HBV infection with no control parameter. That is no vaccination; $(\theta = 0)$, treatment; $(\sigma = 0)$ and vaccine efficacy; $\varepsilon = 0$. We notice that the HBV infection asymptotically approaches zero at a constant rate. This means that without any control strategy, HBV disease cannot be eradicated. However, with a high vaccination rate of 0.6 and vaccine efficacy rate of 1 and without treatment parameter $(\sigma = 0)$, it will take a longer time, say 6 years to eradicate the HBV disease as depicted in Figure 12. We also notice that a high treatment rate of 0.6 with no vaccination parameter $(\theta = 0)$ will only reduce the number of infections but cannot eradicate the HBV infection as depicted in Figure 13. This is because most infected individuals are not aware of their infection and do not seek any medical treatment. Figure 14 also shows a decreasing prevalence of hepatitis B virus infection with a high vaccination rate $(\theta = 0.9)$, high vaccine efficacy rate $(\varepsilon = 1)$ and a high treatment rate $(\sigma = 0.8)$ combined as control strategies. We notice that all the infective compartments (both acutely infected and chronic carriers) population turn to zero in a short time. This means that the disease can be eradicated within the shortest possible time. Thus, this study shows that a combination of treatment and vaccination with a high vaccine efficacy rate as a control strategy is the most effective way of controlling and eradication of hepatitis B virus disease.

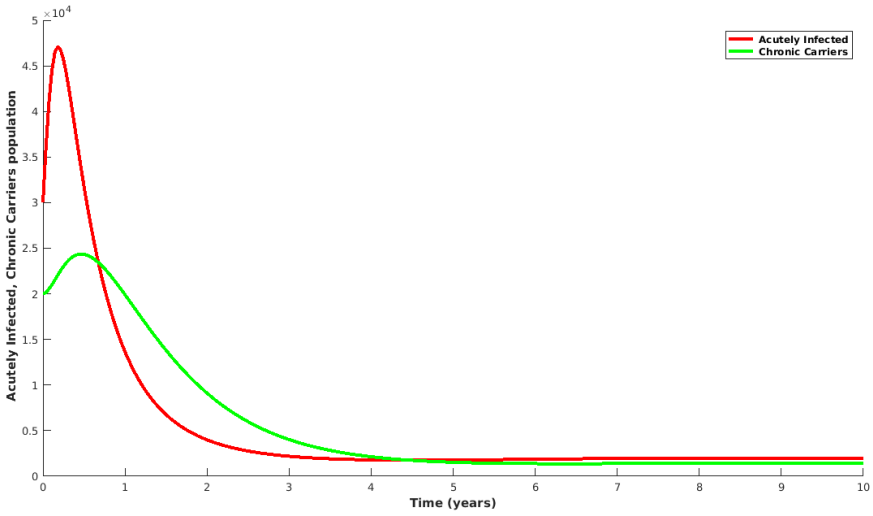

FIGURE 11. Simulation results showing the effect of no control measures such as vaccination rate ($\theta = 0$), vaccine efficacy rate ($\varepsilon = 0$) and treatment rate ($\sigma = 0$) on acutely infected and chronic carriers population and the rest of the parameter values, as stated in Table 1.

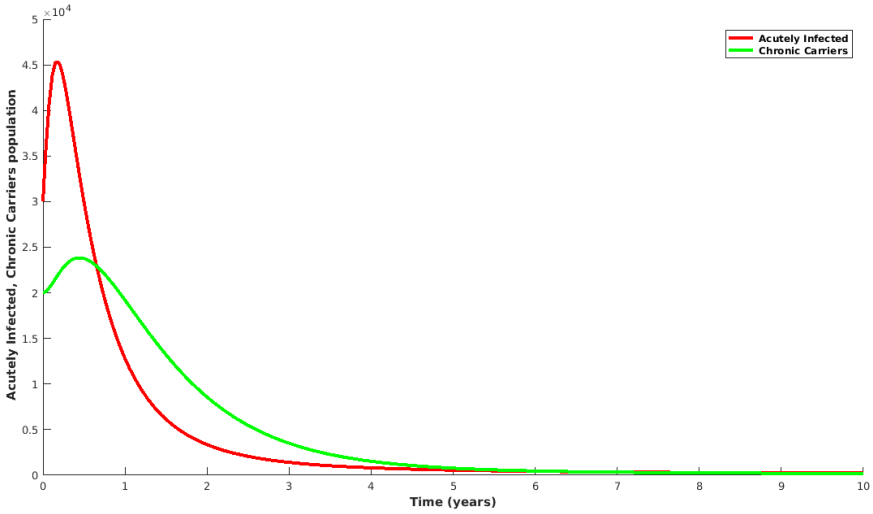

FIGURE 12. Simulation results showing the effect of high vaccination rate ($\theta = 0.6$), strong vaccine efficacy rate ($\varepsilon = 1$) and no treatment rate ($\sigma = 0$) on acutely infected and chronic carriers population and the rest of the parameter values, as stated in Table 1.

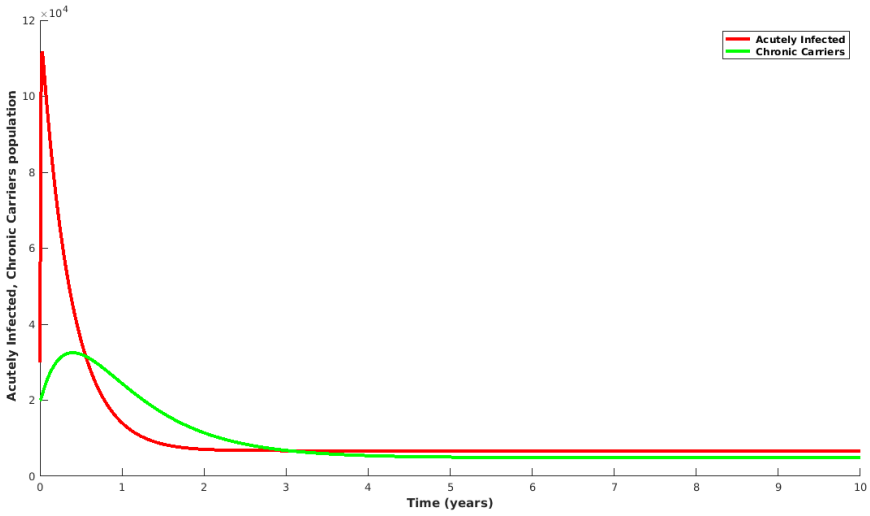

FIGURE 13. Simulation results showing the effect of no vaccination rate ($\theta = 0$), strong vaccine efficacy rate ($\varepsilon = 1$) and a high treatment rate ($\sigma = 6$) on acutely infected and chronic carriers population and the rest of the parameter values, as stated in Table 1.

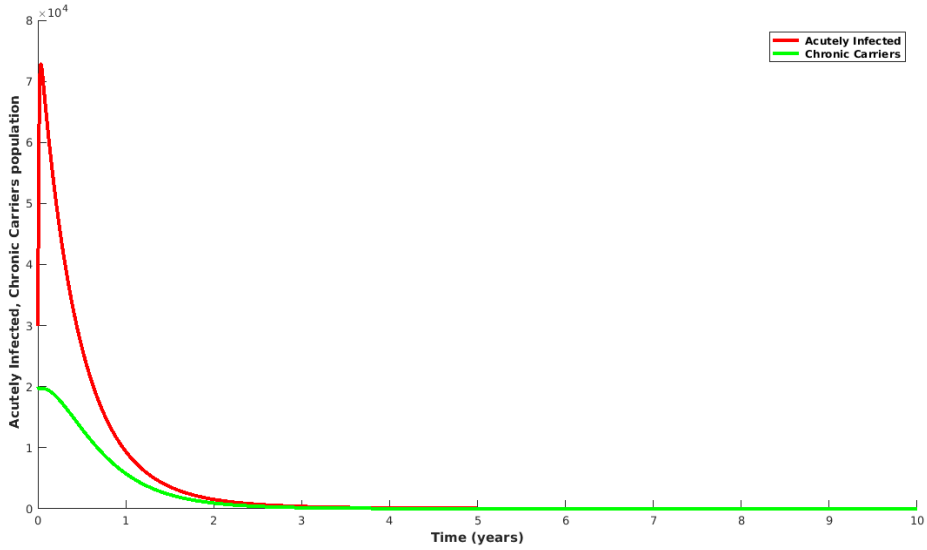

FIGURE 14. Simulation results showing the effect of a very high vaccination rate ($\theta = 0.9$), strong vaccine efficacy rate ($\varepsilon = 1$) and a very high treatment rate ($\sigma = 0.8$) on acutely infected and chronic carriers population and the rest of the parameter values, as stated in Table 1.

5.6. Sensitivity Analysis on the Basic Reproduction Number. The basic reproduction number $\mathbb{R}_0$ is a function of the parameters β, λ, ω, μ_0, μ_1, ψ, ε, θ, $\bar{\omega}$, γ_1, δ, σ, τ_1, τ_2, η_1 and η_2. To control the outbreak of a disease, it is important to control the parameter values that will make $\mathbb{R}_0 < 1$. This is because these parameters contribute most toward the spread of the disease. Hence, we are interested in determining the rate of change of $\mathbb{R}_0$ as the parameter values changes. To consider the variation in the basic reproductive number $\mathbb{R}_0$, we used the approach of Zhang and Zhang [14] and Farman et al [24] to obtain the following partial derivatives:

$$\frac{\partial \mathbb{R}_0}{\partial \beta} = \frac{\lambda(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)][\Psi_0+\Psi_1+\Psi_2]}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0)\Psi_0} \geq 0,$$

$$\frac{\partial \mathbb{R}_0}{\partial \lambda} = \frac{\beta(1-\omega)[(\mu_0+\psi)+\theta(1-\varepsilon)][\Psi_0+\Psi_1+\Psi_2]}{\mu_0(\theta+\mu_0+\psi)(\gamma_1+\tau_1+\mu_0)\Psi_0} \geq 0.$$

The rest of the parameters can be shown in a similar way to determine their sensitivity status with the basic reproduction number, $\mathbb{R}_0$. The results are summarized in Table 2 below.

TABLE 2. Parameters and their relationship with $\mathbb{R}_0$.

Parameter	Relationship	Parameter	Relationship
λ	+	ε	-
β	+	μ_0	-
σ	-	μ_1	-
η_1	+	τ_1	+
η_2	+	τ_2	-
θ	-	δ	+
$\bar{\omega}$	+	ψ	-
ω	-	γ_1	+

5.7. Discussion. In this paper, we extended the model of Zhang and Zhang [14] to incorporate imperfect vaccination and investigated the parameter space that gave rise to the observed patterns of hepatitis B virus transmission dynamics. The increasing use of the hepatitis B vaccine and treating of infected persons has shown a significant impact on the rates of HBV infection and future HBV-related deaths. Analysis from the model system shows that the qualitative behaviours of the model are completely determined by the magnitude of the basic reproductive number $\mathbb{R}_0$. More precisely, when $\mathbb{R}_0 < 1$, the endemic status of the hepatitis B virus disease will naturally settle to the disease-free equilibrium and for that matter, the disease will die out from the entire population. Otherwise, the disease will be uniform persistence and remain to invade the entire population.

Numerical results from the model show that when we increase the proportion of individuals who are vaccinated and the proportion of individuals seeking treatment, the basic reproduction number can be reduced below unity. Hence, $\mathbb{R}_0$ is a decreasing function concerning the vaccination rate and treatment rate indicating that vaccination and treatment are very useful in controlling and total eradication of the hepatitis B virus infections. The model system studied in this paper, however, indicated that the basic reproduction number $\mathbb{R}_0$ which forms the threshold is not enough to completely eradicate the spread of hepatitis B virus infection. This is because the result of the stability analysis investigated show that the model exhibit local asymptotic stability under certain conditions at the disease-free equilibrium provided $\mathbb{R}_0 < 1$ while the stability of the endemic equilibrium examined using the centre manifold theory proved the existence of a backward bifurcation phenomenon under certain conditions.

It was also noticed that the model system settles at the disease-free equilibrium state with a very strong vaccine efficacy rate, $\varepsilon = 1$ and both the vaccination rate, θ and treatment rate, σ having values 0.4 and 0.6 respectively. Thus, vaccination of susceptible individuals and treatment of infected individuals play an important role in controlling the hepatitis B virus disease. Although total eradication of the hepatitis B virus disease remains a global problem, base on the finding of this study, we suggested that a combination of massive vaccination and treatment of infected individuals to the highest level should be included in government hepatitis B virus

control programmes. However, vaccines with a very strong vaccine efficacy rate should be used to help eradicate this deadly disease.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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