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MATHEMATICAL ANALYSIS OF HEPATITIS B TRANSMISSION MODEL

OUEDRAOGO Boukary[1,*], ZOROM Malicki[2] and GOUBA Elisée[1]

[1]Laboratoire d'Analyse Numérique d'Informatique
et de Biomathématiques (LANIBIO)
Département de Mathématiques
Université Joseph KI ZERBO
Burkina Faso
e-mail: aboubakrrambo1930@gmail.com
elgouba@gmail.com

[2]Institut International d'ingénierie de l'Eau et de l'Environnement (2iE)
Burkina Faso
e-mail: malicki.zorom@2ie-edu.org

Abstract

In this article, we present the transmission dynamics of the acute and chronic hepatitis B epidemic problem. To control the spread of hepatitis in a community, we first develop a mathematical model

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*Corresponding author

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for the transmission of the virus of hepatitis B. After framing the mathematical model, we show the existence and uniqueness of the solution, then mathematically analyze the model and determine the disease-free equilibrium state of the model. Besides, we determine the basic reproduction number $\mathcal{R}_0$ for this model which is interpreted epidemiologically. Next, we study the local stability of the disease-free-equilibrium state and show that if $\mathcal{R}_0 < 1$, then, the disease-free equilibrium is asymptotically stable, otherwise unstable. Finally, a sensitivity analysis is performed to determine the relative importance of the model parameters to disease transmission and prevalence. The paper ends with the numerical simulation to illustrate the theoretical results.

1. Introduction

The liver is one of the most important organs in the human body and its infection causes different diseases like hepatitis B. Hepatitis B is one of the most common viral diseases across the world. The risk of becoming chronic that leads to the appearance of liver cancer or cirrhosis of the liver makes it a serious pathology. Viral hepatitis B is an inflammatory disease of the liver caused by the hepatitis B virus. Hepatitis B is a transmissible virus that can cause liver ulcerations, liver failure, and liver diseases like cirrhosis or liver cancer. It is transmitted sexually but also with the contact of biological fluids (the blood, the semen, the love juice ...) in small communities. For example, in the family environment, the virus is highly contagious. The hepatitis B virus reservoir appears to be strictly human and the virus can resist in the external environment for more than 7 days [1]. Hepatitis B is difficult to treat. Most of the infected people will not have any symptoms of the infection. They are called *asymptomatic carriers*, they play an important role in the transmission of this disease. Hepatitis B manifests in two forms, acute (short term: 6 months) or chronic (long term: beyond 6 months) [1]. When a person is first infected with the hepatitis B virus, he develops an “acute” infection. This acute infection can present different forms of symptoms. The acute symptoms can often be mild and may be similar (mistakenly) to those of flu. These manifest by fatigue, joint pains, pains in the stomach area, a

loss of appetite, nausea and a general feeling of being unwell. In some cases, hepatitis B can also cause jaundice, which is a sign of liver dysfunction. It is also possible that the infected person does not manifest any symptom.

The proportion of symptomatic cases of acute hepatitis B increases with age while the risk of transition to chronic infection decreases.

The goal of the treatment against the chronic viral hepatitis B is to improve the survival and the quality of patients' lives and prevent the spread of the disease to cirrhosis or to liver cancer and to death.

The vertical transmission being the frequent mode of HBV contamination in countries with high endemicity, screening during pregnancy is one of the most effective ways of its elimination.

In 1927, Kermack and McKendrik [14] applied Ross' ideas and studied the transmission of an infectious disease in humans. In 1991, Anderson and May [15] described the effect of carriers on HBV transmission using a simple deterministic model. Nokes et al. [16] presented a model for the dynamism of hepatitis B transmission. Medley et al. [17] used a mathematical model for the elimination of HBV in New Zealand. Khan et al. [2] presented an age-structured model for the prediction of the transmission of HBV and evaluated the long-term effectiveness of the vaccination program in China.

In this article, we first develop a model of HBV transmission.

The articles [2] and [3] made it possible to make the following modifications which are not taken into account in the model of Medley et al. [17].

An interaction between the cured compartment and that of the susceptible, that is to say that the cured people lose their immunities and become sensitive again.

The infectious class is divided into two stages, such as acute infectious stage and chronic infectious stage. So the total population is divided into five compartments, namely, $S(t)$ susceptible, $E(t)$ exposed, $I_1(t)$ infected by

acute hepatitis B, $I_2(t)$ infected with chronic hepatitis B, and $R(t)$ recovered. After formulating the model, we determine the basic reproduction number $\mathcal{R}_0$ and disease-free steady state. We prove that under certain conditions, the model is stable. Next, a sensitivity analysis is performed to determine the relative importance of the model parameters to disease transmission and prevalence. Finally, the theoretical results of the analysis are illustrated by a numerical simulation and we end the paper with a conclusion.

2. Formulation of the Model

In this section, we develop a mathematical model for HBV transmission. The diagram of HBV dynamics that we propose for our study is a compartmental model (SEIR), like that of Medley et al. [17] to which modifications have been made.

The introduction of vertical transmission decreases the births by an amount bI_2p_1 which no longer becomes susceptible because the newborns resulting from these births become chronic with the vertical transmission, which causes the appearance of this quantity bI_2p_1 at the level of the chronic compartment I_2.

We constructed our diagram by also taking into account the biology of HBV and its natural history. Thus, we have the following diagram:

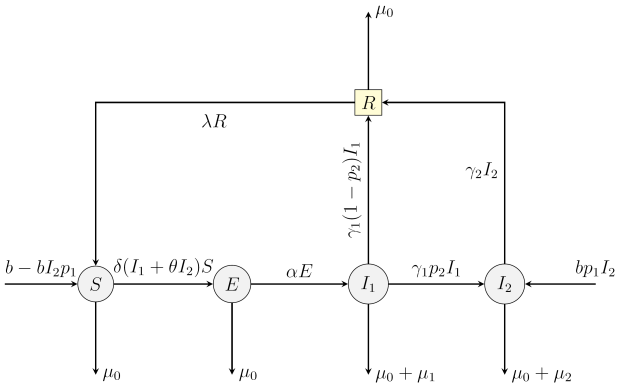

Figure 1. Flow chart of the model of HBV transmission.

The model represented by Figure 1, composed of five compartments S, E, I_1, I_2 and R represents, respectively, the susceptibles' compartment, latent infections, acute infections, chronic carriers and recoveries.

$\delta(I_1 + \theta I_2)S$ indicates the horizontal transmission from class S to class E, where δ is the contact rate and θ the contagiousness of chronic carriers compared to acute infections;

$bp_1 I_2$ denotes the vertical transmission of I_2 to I_2 through the birth of an individual's offspring chronic carrier, where b is the birth rate of the population and p_1 the proportion of newborns chronic carriers who are infected through vertical transmission;

$b - bp_1 I_2$ is the flux entering the sensitive class;

αE designates the transition from compartment E to that of I_1, where α is the acute infection rate of exposed individuals;

$\gamma_2 I_2$ shows the healing of chronic carriers and therefore the passage from compartment I_2 to R, where γ_2 is the proportion of acutely infected individuals who become chronic carriers;

λR indicates the progressive loss of immunity of cured individuals who pass to the S compartment, where λ is the rate of loss of immunity of cured individuals;

$p_2 \gamma_1 I_1$ shows the proportion of acutely infected individuals who become chronic carriers, where γ_1 is the cure rate of acutely infected;

$(1 - p_2)\gamma_1 I_1$ shows the proportion of acutely infected individuals who clear HBV and go from I_1 to R, where $(1 - p_2)$ is the proportion of acutely infected individuals who clear HBV;

μ_0 is the natural mortality;

μ_1 denotes mortality due to acute HBV infection;

μ_2 denotes mortality due to chronic HBV infection.

Remark. • The population of newborn chronic carriers, born of chronic carriers is lower to the sum of the deaths of chronic carriers and the population passing from the state of chronic carriers to the state of recovery [5]. In this case, we have $bp_1 < \mu_0 + \mu_2 + \gamma_2$, otherwise the chronic carriers would continue to increase rapidly as long as there is infection that is to say $\frac{dI_2}{dt} > 0$ for $I_2 \neq 0$ or $I_1 \neq 0$ and $t \geq 0$.

• The adequate contact is inferior to sum of the acute hepatitis B mortality rate, to the recovery of acutely infected individuals and at the contact rate, that is to say $\alpha\delta b < \mu_0 + \mu_1 + \gamma_1 + \alpha$ because 95% of cases of acute infection evolve towards spontaneous healing.

Thus, we have the following dynamic model:

$$\begin{cases} \frac{dS(t)}{dt} = b - bp_1 I_2(t) - \delta(I_1(t) + \theta I_2(t))S(t) - \mu_0 S(t) + \lambda R(t), \\ \frac{dE(t)}{dt} = \delta(I_1(t) + \theta I_2(t))S(t) - (\mu_0 + \alpha)E(t), \\ \frac{dI_1(t)}{dt} = \alpha E(t) - (\mu_0 + \mu_1 + \gamma_1)I_1(t), \\ \frac{dI_2(t)}{dt} = \gamma_1 p_2 I_1(t) + bp_1 I_2(t) - (\mu_0 + \mu_2 + \gamma_2)I_2(t). \\ \frac{dR(t)}{dt} = \gamma_2 I_2(t) + \gamma_1(1 - p_2)I_1(t) - \lambda R(t) - \mu_0 R(t) \end{cases} \quad (1)$$

with the initial conditions

$$S(0) \geq 0; \quad E(0) \geq 0; \quad I_1(0) \geq 0; \quad I_2(0) \geq 0; \quad R(0) \geq 0.$$

3. Well Posedness of the System (1)

The following theorem shows that the model is well-posed.

Theorem 1. *The solutions of system* (1) *are bounded for* $t \geq 0$ *that is to say*:

$$N(t) \leq e^{-\mu_0 t}\left(\frac{b}{\mu_0} e^{\mu_0 t} + c\right), \quad c \in \mathbb{R}.$$

By letting t tend to $+\infty$,

$$N \leq \frac{b}{\mu_0} < \infty \text{ which gives: } S + E + I_1 + I_2 + R \leq \frac{b}{\mu_0} < \infty,$$

where $N = S + E + I_1 + I_2 + R$.

Proof. We assume that the population is closed, i.e.,

$$N(t) = S(t) + E(t) + I_1(t) + I_2(t) + R(t),$$

which on differentiation and simplification gives

$$\frac{dN(t)}{dt} = b - \mu_0(S(t) + E(t) + I_1(t) + I_2(t) + R(t)) - \mu_1 I_1(t) - \mu_2 I_2(t).$$

We then get

$$\frac{dN(t)}{dt} + \mu_0 N(t) + \mu_1 I_1(t) + \mu_2 I_2(t) = b.$$

And finally,

$$\frac{dN(t)}{dt} + \mu_0 N(t) < b \tag{2}$$

because $\mu_1 > 0$, $\mu_2 > 0$, $I_1 > 0$ and $I_2 > 0$.

Let $\frac{dN(t)}{dt} + \mu_0 N(t) = 0$ be the homogeneous equation associated with the differential inequality (2).

The solution of our homogeneous equation is: $N(t) = ke^{-\mu_0 t}$, $k \in \mathbb{R}$.

Using the method of variation of constants, we have

$$k'(t)e^{-\mu_0 t} - \mu_0 k(t)e^{-\mu_0 t} + \mu_0 k(t)e^{-\mu_0 t} = b \Rightarrow k'(t)e^{-\mu_0 t} = b,$$

or $k'(t) = be^{\mu_0 t}$, and after integration, we have: $k(t) = \frac{b}{\mu_0} e^{\mu_0 t} + c$, $c \in \mathbb{R}$ as $\frac{dN(t)}{dt} + \mu_0 N(t) < b$, so $N(t) \leq \left(\frac{b}{\mu_0} e^{\mu_0 t} + c\right) e^{-\mu_0 t}$, i.e., $N(t) \leq \frac{b}{\mu_0} +$

$ce^{-\mu_0 t}$, where c is a constant. By letting t tend to $+\infty$, we have

$$N \leq \frac{b}{\mu_0} < \infty$$

which completes the proof.

Next, we restrict our study to the following set π:

$$\pi = \left\{ (S,\ E,\ I_1,\ I_2,\ R)^t \in \mathbb{R}_+^5 \ \middle|\ S + E + I_1 + I_2 + R \leq \frac{b}{\mu_0} \right\}. \tag{3}$$

The set π is positively invariant. Therefore, the system is mathematically well-posed. Then for the initial starting point $x \in \mathbb{R}_+^5$, the trajectory is located in π. Therefore, we will focus our attention only on the π region.

Proposition 1. *The model* (1) *has a unique disease-free equilibrium point* E_0 *in* π *such that* $E_0 = \left(\frac{b}{\mu_0},\ 0,\ 0,\ 0,\ 0 \right)$.

Proof. In considering model (1), there is no disease in the population if the variables E, I_1 and I_2 are zero, that is to say no infection in the population.

Let E_0 be the disease-free equilibrium point commonly called *DFE* (*disease-free equilibrium*). For the system (1), replacing E, I_1 and I_2 by 0, we obtain

$$\begin{cases} \dfrac{dS(t)}{dt} = b - \mu_0 S(t) + \lambda R(t), \\ \dfrac{dR(t)}{dt} = -\lambda R(t) - \mu_0 R(t). \end{cases} \tag{4}$$

A disease-free equilibrium point is in the form $E_0 = (S_0,\ 0,\ 0,\ 0,\ R^0)$ with $R^0 = 0$ because there is no postponement because there were no sick people.

And then $(S_0, 0, 0, 0, 0)$ is the solution of the system:

$$\begin{cases} \dfrac{dS(t)}{dt} = b - \mu_0 S(t) + \lambda R(t), \\ -(\lambda + \mu_0) R(t) = 0. \end{cases} \tag{5}$$

Since $\dfrac{dS(t)}{dt} = 0,\ b - \mu_0 S_0 = 0.$ Thus, $S_0 = \dfrac{b}{\mu_0}.$

4. Basic Reproduction Number

The basic reproduction number $\mathcal{R}_0$ of model (1) is given as follows:

$$\mathcal{R}_0 = \frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1)}. \tag{6}$$

It can be proved by using the notation of van den Driessche and J. Watmough [9] taken up by Sallet [4]. Indeed, we have

$$F = \begin{bmatrix} 0 & \delta S_0 & \delta\theta S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} -(\mu_0 + \alpha) & 0 & 0 \\ \alpha & -(\mu_0 + \mu_1 + \gamma_1) & 0 \\ 0 & \gamma_1 p_2 & bp_1 - (\mu_0 + \mu_2 + \gamma_2) \end{bmatrix},$$

$$\det(V) = (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)[bp_1 - (\mu_0 + \mu_2 + \gamma_2)].$$

Since $\det(V) \neq 0$, V is invertible and its inverse is

$$V^{-1} = \begin{bmatrix} -\frac{1}{\mu_0+\alpha} & 0 & 0 \\ -\frac{\alpha}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)} & -\frac{1}{(\mu_0+\mu_1+\gamma_1)} & 0 \\ -\frac{\alpha\gamma_1 p_2}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)\cdot(\mu_0+\mu_2+\gamma_2-bp_1)} & -\frac{\gamma_1 p_2}{(\mu_0+\mu_1+\gamma_1)\cdot(\mu_0+\mu_2+\gamma_2-bp_1)} & -\frac{1}{(\mu_0+\mu_2+\gamma_2-bp_1)} \end{bmatrix},$$

$$-FV^{-1} = \begin{bmatrix} K_1 & K_2 & K_3 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

with

$$K_1 = \frac{\alpha\delta S_0}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)} + \frac{\delta\theta S_0\alpha\gamma_1 p_2}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)(\mu_0+\mu_2+\gamma_2-bp_1)},$$

$$K_2 = \frac{\delta S_0}{(\mu_0+\mu_1+\gamma_1)} + \frac{\delta\theta S_0\gamma_1 p_2}{(\mu_0+\mu_1+\gamma_1)(\mu_0+\mu_2+\gamma_2-bp_1)},$$

$$K_3 = \frac{\delta\theta S_0}{\mu_0+\mu_2+\gamma_2-bp_1}.$$

The characteristic polynomial of $-FV^{-1}$ is: $P(z) = z^2(K_1 - z)$.

The eigenvalues are as follows:

$$z_1 = z_2 = 0, \text{ and}$$

$$z_3 = \frac{\alpha\delta S_0}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)} + \frac{\delta\theta S_0\alpha\gamma_1 p_2}{(\mu_0+\alpha)(\mu_0+\mu_1+\gamma_1)(\mu_0+\mu_2+\gamma_2-bp_1)}.$$

Therefore,

$$\mathcal{R}_0 = \frac{\alpha\delta S_0}{(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)} + \frac{\delta\theta S_0 \alpha\gamma_1 p_2}{(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1)}$$

which means

$$\mathcal{R}_0 = \frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1)}.$$

We know that $bp_1 < \mu_0 + \mu_2 + \gamma_2$, that is to say $\mu_0 + \mu_2 + \gamma_2 - bp_1 > 0$ so $\mathcal{R}_0 > 0$.

5. Local Stability

The stability of the steady state without disease E_0 is governed by the reproduction basic number of $\mathcal{R}_0$.

Proposition 2. *The equilibrium* $E_0 = \left(\frac{b}{\mu_0}, 0, 0, 0, 0\right)$ *is locally asymptotically stable if* $\mathcal{R}_0 < 1$ *and unstable if* $\mathcal{R}_0 > 1$.

Proof. Let $f(S, E, I_1, I_2, R) = (f_1, f_2, f_3, f_4, f_5)$, where

$$f_1 = b - bp_1 I_2(t) - \delta(I_1(t) + \theta I_2(t))S(t) - \mu_0 S(t) + \lambda R(t);$$

$$f_2 = \delta(I_1(t) + \theta I_2(t))S(t) - (\mu_0 + \alpha)E(t);$$

$$f_3 = \alpha E(t) - (\mu_0 + \mu_1 + \gamma_1)I_1(t);$$

$$f_4 = \gamma_1 p_2 I_1(t) + bp_1 I_2(t) - (\mu_0 + \mu_2 + \gamma_2)I_2(t);$$

$$f_5 = \gamma_2 I_2(t) + \gamma_1(1 - p_2)I_1(t) - \lambda R(t) - \mu_0 R(t);$$

$$J_f = \begin{pmatrix} \frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial E} & \frac{\partial f_1}{\partial I_1} & \frac{\partial f_1}{\partial I_2} & \frac{\partial f_1}{\partial R} \\ \frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial E} & \frac{\partial f_2}{\partial I_1} & \frac{\partial f_2}{\partial I_2} & \frac{\partial f_2}{\partial R} \\ \frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial E} & \frac{\partial f_3}{\partial I_1} & \frac{\partial f_3}{\partial I_2} & \frac{\partial f_3}{\partial R} \\ \frac{\partial f_4}{\partial S} & \frac{\partial f_4}{\partial E} & \frac{\partial f_4}{\partial I_1} & \frac{\partial f_4}{\partial I_2} & \frac{\partial f_4}{\partial R} \\ \frac{\partial f_5}{\partial S} & \frac{\partial f_5}{\partial E} & \frac{\partial f_5}{\partial I_1} & \frac{\partial f_5}{\partial I_2} & \frac{\partial f_5}{\partial R} \end{pmatrix}.$$

That is to say,

$$J_f = \begin{pmatrix} -\delta(I_1 + \theta I_2) - \mu_0 & 0 & -\delta S & -(bp_1 + \delta\theta S) & \lambda \\ \delta(I_1 + \theta I_2) & -(\mu_0 + \alpha) & \delta S & \delta\theta S & 0 \\ 0 & \alpha & -(\mu_0 + \mu_1 + \gamma_1) & 0 & 0 \\ 0 & 0 & \gamma_1 p_2 & bp_1 - (\mu_0 + \mu_2 + \gamma_2) & 0 \\ 0 & 0 & \gamma_1(1 - p_2) & \gamma_2 & -(\mu_0 + \lambda) \end{pmatrix}, \tag{7}$$

$$J_f(E_0) = \begin{pmatrix} -\mu_0 & 0 & -\frac{\delta b}{\mu_0} & -\left(bp_1 + \frac{\delta\theta b}{\mu_0}\right) & \lambda \\ 0 & -(\mu_0 + \alpha) & \frac{\delta b}{\mu_0} & \frac{\delta\theta b}{\mu_0} & 0 \\ 0 & \alpha & -(\mu_0 + \mu_1 + \gamma_1) & 0 & 0 \\ 0 & 0 & \gamma_1 p_2 & bp_1 - (\mu_0 + \mu_2 + \gamma_2) & 0 \\ 0 & 0 & \gamma_1(1 - p_2) & \gamma_2 & -(\mu_0 + \lambda) \end{pmatrix} \tag{8}$$

or

$$J_f(E_0) = -\mu_0[-(\mu_0 + \lambda)] \begin{pmatrix} -(\mu_0 + \alpha) & \frac{\delta b}{\mu_0} & \frac{\delta\theta b}{\mu_0} \\ \alpha & -(\mu_0 + \mu_1 + \gamma_1) & 0 \\ 0 & \gamma_1 p_2 & -(\mu_0 + \mu_2 + \gamma_2 - bp_1) \end{pmatrix}. \tag{9}$$

Two eigenvalues z_1 and z_2 of $Jf(E_0)$ are negative, $z_1 = -\mu_0$ and $z_2 = -(\mu_0 + \lambda)$. For the rest of eigenvalues, we consider the following 3×3 matrix:

$$B = \begin{pmatrix} -(\mu_0 + \alpha) & \dfrac{\delta b}{\mu_0} & \dfrac{\delta\theta b}{\mu_0} \\ \alpha & -(\mu_0 + \mu_1 + \gamma_1) & 0 \\ 0 & \gamma_1 p_2 & -(\mu_0 + \mu_2 + \gamma_2 - bp_1) \end{pmatrix}. \quad (10)$$

The characteristic polynomial of the matrix B is given by

$$\begin{aligned} P(z) = {} & -z^3 - z^2[(\mu_0 + \mu_2 + \gamma_2 - bp_1) + (\mu_0 + \alpha) + (\mu_0 + \mu_1 + \gamma_1)] \\ & - z\Big[(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1) + (\mu_0 + \alpha)(\mu_0 + \mu_2 + \gamma_2 - bp_1) \\ & \quad + (\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1) - \frac{\alpha\delta b}{\mu_0}\Big] \\ & + \frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0} \\ & - (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1). \end{aligned}$$

We then obtain the following characteristic equation:

$$\begin{aligned} & z^3 + z^2[(\mu_0 + \mu_2 + \gamma_2 - bp_1) + (\mu_0 + \alpha) + (\mu_0 + \mu_1 + \gamma_1)] \\ & + z\Big[(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1) + (\mu_0 + \alpha)(\mu_0 + \mu_2 + \gamma_2 - bp_1) \\ & + (\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1) - \frac{\alpha\delta b}{\mu_0}\Big] \\ & - \frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0} \\ & + (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1) = 0. \end{aligned}$$

Set

$$a_1 = (\mu_0 + \mu_2 + \gamma_2 - bp_1) + (\mu_0 + \alpha) + (\mu_0 + \mu_1 + \gamma_1),$$

$$a_2 = (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1) + (\mu_0 + \alpha)(\mu_0 + \mu_2 + \gamma_2 - bp_1) + (\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1) - \frac{\alpha\delta b}{\mu_0}$$

and

$$a_3 = -\frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0} + (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1).$$

Then

$$a_1 = (\mu_0 + \mu_2 + \gamma_2 - bp_1) + (\mu_0 + \alpha) + (\mu_0 + \mu_1 + \gamma_1),$$

$a_1 > 0$ because $(\mu_0 + \mu_2 + \gamma_2 - bp_1) > 0$, $(\mu_0 + \alpha) > 0$ and $(\mu_0 + \mu_1 + \gamma_1) > 0$,

$$a_2 = (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1) + (\mu_0 + \mu_2 + \gamma_2 - bp_1)(2\mu_0 + \mu_1 + \gamma_1 + \alpha) - \frac{\alpha\delta b}{\mu_0},$$

$a_2 > 0$ because $\alpha\delta b < \mu_0 + \mu_1 + \gamma_1 + \alpha$.

Therefore, it is obvious that

$$(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1) + (\mu_0 + \mu_2 + \gamma_2 - bp_1)(\mu_0 + \mu_1 + \gamma_1 + \alpha) > \frac{\alpha\delta b}{\mu_0},$$

$$a_3 = -\frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0} + (\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1)$$

$$= -\frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)(\mu_0 + \mu_2 + \gamma_2 - bp_1)} + 1,$$

$$a_3 = -\mathcal{R}_0 + 1,$$

$a_3 > 0$ if $\mathcal{R}_0 < 1$,

$$a_1 a_2 - a_3 = (\mu_0 + \mu_2 + \gamma_2 - bp_1)$$
$$\cdot \left[(\mu_0 + \mu_2 + \gamma_2 - bp_1)(2\mu_0 + \mu_1 + \gamma_1 + \alpha) - \frac{\alpha\delta b}{\mu_0} \right]$$
$$+ a_2[(\mu_0 + \alpha)(\mu_0 + \mu_1 + \gamma_1)]$$
$$+ \frac{\alpha\delta b(\mu_0 + \mu_2 + \gamma_2 - bp_1) + \alpha\gamma_1 p_2 \delta\theta b}{\mu_0},$$

$a_1 a_2 - a_3 > 0$ because adequate contact is known to be less than the sum of the mortality rate due to acute hepatitis B, to the cure rate of acutely infected individuals and the contact rate, that is to say that $\alpha\delta b < \mu_0 + \mu_1 + \gamma_1 + \alpha$, and hence $(\mu_0 + \mu_2 + \gamma_2 - bp_1)(2\mu_0 + \mu_1 + \gamma_1 + \alpha) - \frac{\alpha\delta b}{\mu_0} > 0$ and $a_2 > 0$.

It results from the Routh-Hurwitz [10] criteria that the eigenvalues of the matrix B have also real negative parts because $a_1 > 0$, $a_1 a_2 - a_3 > 0$ and $a_3 > 0$ if $\mathcal{R}_0 < 1$. Consequently, the equilibrium without disease of model (1) is locally and asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

6. Sensitivity Analysis

In determining how best to tackle hepatitis B and reduce hepatitis B mortality, it is necessary to know the relative importance of the different factors responsible for its transmission and prevalence. Initial disease transmission is directly related to $\mathcal{R}_0$, and disease prevalence is directly related to the disease-free equilibrium point [11].

Sensitivity analysis tells us how important each parameter is to disease transmission. Such information is crucial not only for experimental design, but also to data assimilation and reduction of complex nonlinear models [12].

Definition. The *normalized forward sensitivity index* of a variable u that depends continuously on a parameter p is defined as:

$$\gamma_p^u = \frac{\partial u}{\partial p} \cdot \frac{p}{u}.$$

Sensitivity analysis is also commonly used to determine the robustness of model predictions to parameter values, as there are usually errors in data collection and presumed parameter values. However, as we do not use our model to make predictions, we do not utilize this aspect of sensitivity analysis.

Table 1. Baseline values of the parameters used in sensitivity analysis and numerical simulation

Parameters	Descriptions	Values	Reference
b	Population birth rate	0.000121	[3]
δ	Contact or transmission rate	0.8-20.49	[3]
θ	Infectiousness of carriers relative to acute infections	0.1	[3]
α	Rate of moving from exposed to acute	6	[3]
γ_1	Cure rate of acutely infected individuals	4	[3]
γ_2	Cure rate of chronic carriers	0.06	[2]
λ	Rate of loss of immunity of cured individuals	0.03-0.06	[3]
p_1	Proportion of neonates of chronic carriers who are infected by vertical transmission	0.11	[3]
p_2	Proportion of acutely infected individuals who become chronic carriers	0.05-0.9	[3]
$1-p_2$	Proportion of acuted infected individuals who clear HBV	0.1-0.95	assumed
μ_0	Natural mortality rate	$1/(365 \times 60)$	assumed
μ_1	Mortality rate due to acute HBV infection	0.002-0.004	[2]
μ_2	Mortality rate due to chronic HBV infection	0.5	[2]
S_0	Sensitive individuals	100	[13]
E_0	Exposed individuals	30	[13]
I_1	Acute infected individuals	20	[13]
I_2	Chronic HBV carriers	5	[13]
R^0	Recovered individuals	10	[13]

Table 2. Variables used in the model

Variables	Biological description
S	Individuals susceptibles to contracting the disease
E	Latent infected individuals who will progress to an acutely infected state
I_1	Acute infected individuals
I_2	Chronically infected individuals
R	Cured individuals likely to lose immunity
N	Total population: $N = S + E + I_1 + I_2 + R$

As we have an explicit expression for $\mathcal{R}_0$, we can evaluate the sensitivity of $\mathcal{R}_0$ to the eleven different parameters described in Table 1 as, $\gamma_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p} \cdot \frac{p}{\mathcal{R}_0}$ to provide an analytical expression for the sensitivity index [11].

Given the explicit formula (5) for $\mathcal{R}_0$, we can easily derive an analytical expression for the sensitivity of $\mathcal{R}_0$ with respect to each parameter that comprises it. The obtained values are described in Table 1, which presents the sensitivity indices for the baseline parameter values that we use for numerical analysis.

Table 3. Sensitivity indices of $\mathcal{R}_0$ to parameters for baseline parameter values given in Table 1 for the parameters depending of $\mathcal{R}_0$

Parameters	Sensitivity index
b	+1
δ	+1
θ	+0.0345
α	$+7.6103e^{-6}$
γ_1	–0.7366
γ_2	–0.0282
p_1	$+6.2541\ e^{-6}$
p_2	+0.2631
μ_0	–1
μ_1	$-2.4993\ e^{-4}$
μ_2	–0.2349

After the sensitivity analysis of $\mathcal{R}_0$, we find that the sensitive parameters are b and δ. These parameters must be estimated carefully because a small variation in these parameters will cause large quantitative changes.

As the disease-free equilibrium E_0 depends only on b and μ_0, then these parameters are also the sensitive parameters of E_0.

7. Numerical Simulation

In this section, we verify some of our analytical results by using the numerical method. The simulation of our article must be considered from a qualitative point of view but not from a quantitative point of view.

The parameters used in the numerical simulations are collected from the literature and some are assumed with biologically achievable values (see Table 1).

The initial conditions S_0, E_0, $I_{1.0}$, $I_{2.0}$ and R_0 are all positive.

Here, we offer to view the numerical simulations of model (1). The acknowledged graphs portray the dynamics of the susceptible population, the latent population, the HBV acute infected population, the chronic population, and the recovered population, respectively.

Consequently, we acquired the results shown in Figures 2 to 7.

In Figure 2, the graph shows that the susceptible population first decreases because individuals become infected with hepatitis B and then increases over time because recovered individuals gradually lose their immunity and become susceptible again.

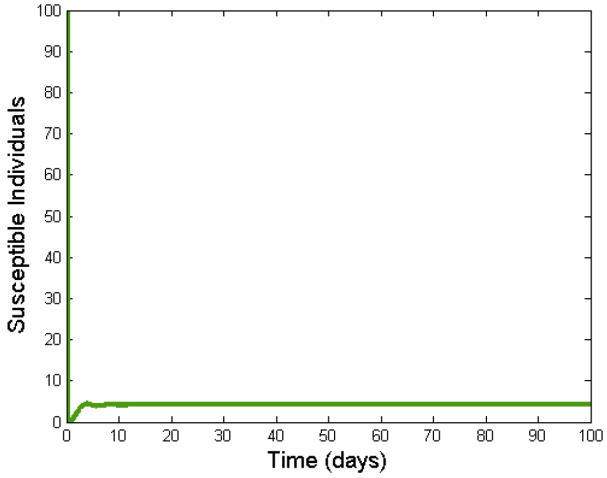

Figure 2. The plot appears as the dynamics of hepatitis B susceptible individuals $S(t)$.

In Figure 3, the latent population gradually decreases over time as shown in the plot because it moves into the acutely infected compartment.

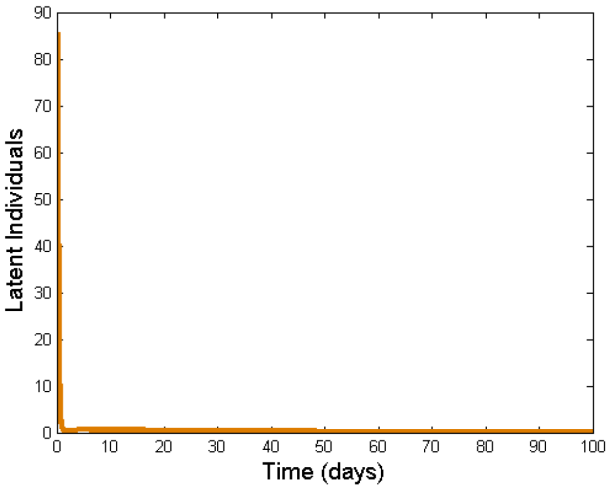

Figure 3. The plot shows the dynamics of hepatitis B latent individuals $E(t)$.

In Figure 4, acutely infected individuals also gradually decrease over time as the plot appears as they progress to either the chronic or the recovered compartment.

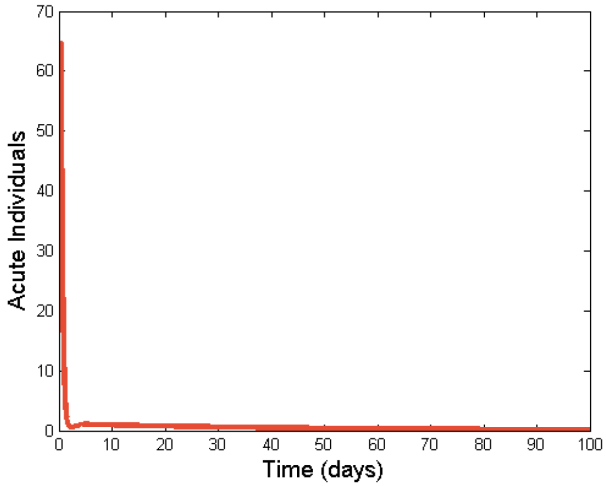

Figure 4. The plot represents the dynamics of hepatitis B acute infected individuals $I_1(t)$.

In Figure 5, the chronic individuals also gradually decrease over time as the plot indicates because they evolve into the recovered compartment.

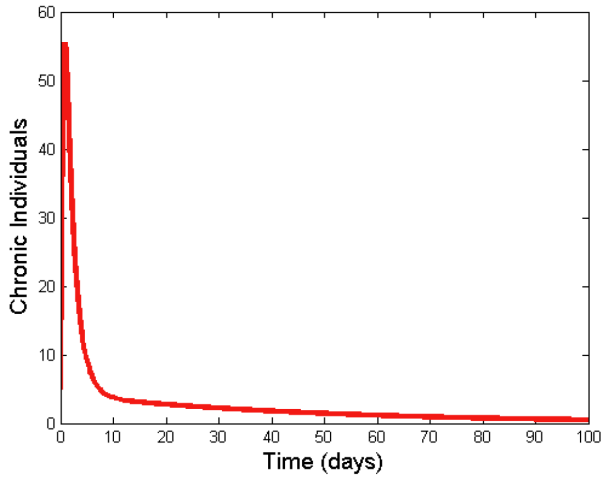

Figure 5. The plot appears the dynamics of hepatitis B chronic individuals $I_2(t)$.

In Figure 6, the recovered individuals gradually increase and then decrease over time as shown in the plot because they move into the compartment of susceptible individuals.

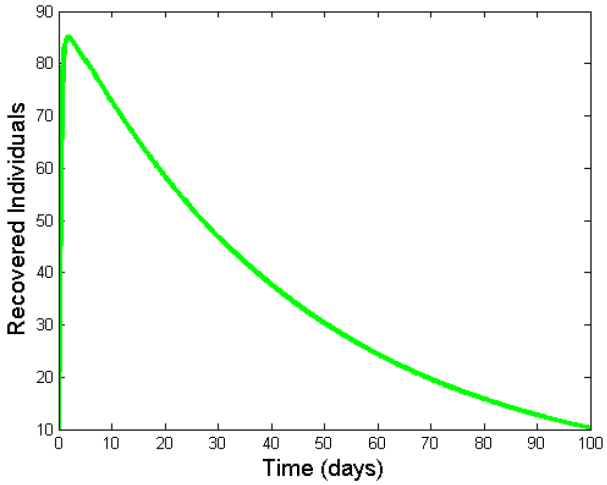

Figure 6. The plot shows the dynamics of hepatitis B recovered individuals $R(t)$.

In Figure 7, we summarize the dynamics of susceptible, latent, acute, chronic, and recovered individuals.

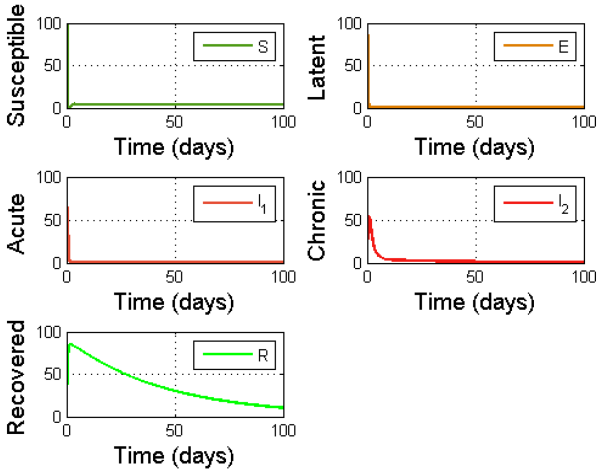

Figure 7. The plot shows the dynamics of hepatitis B for all five compartments.

The decrease in individuals in the latent, acute and chronic infected compartments shows that the disease will disappear over time. The increase in individuals in the recovered compartment shows that individuals recover from hepatitis B but the decrease shows that these recovered individuals gradually lose their immunities and become susceptible again, hence the increase in individuals in the susceptible class.

8. Conclusion

In this paper, a deterministic model is formulated to describe hepatitis B virus transmission in a population. After formulating the model, we found the basic reproduction number $\mathcal{R}_0$ which made possible to predict whether the disease will disappear $(\mathcal{R}_0 < 1)$ or persist $(\mathcal{R}_0 > 1)$. Sensitivity analysis shows that parameters b, δ and μ_0, i.e., respectively, the population birth rate, the transmission rate and the natural mortality rate are sensitive parameters and a small variation of these will lead to a large change in disease transmission dynamics. The numerical simulation has permitted to confirm the theoretical results obtained from the analysis. The numerical results also showed that latent, acute and chronic infected individuals recover spontaneously or after medical intervention but gradually lose their immunity and become susceptible again. Some medical research must be carried out in order to allow individuals recovered of hepatitis B to retain their immunity for life.

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