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► **To cite this version:**

Hamadjam Abboubakar. Fractional Dynamics of a Hepatitis B Virus Transmission Model with Imperfect Vaccine. 2024. hal-04673414

HAL Id: hal-04673414

<https://hal.science/hal-04673414v1>

Preprint submitted on 20 Aug 2024

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Fractional Dynamics of a Hepatitis B Virus Transmission Model with Imperfect Vaccine

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Abstract

The objective of this work is to derive and study a model of transmission dynamics of hepatitis B virus (HBV) with integer and fractional derivatives in the Caputo sense. After the formulation the models, we perform an asymptotic stability analysis of the disease-free equilibrium point of both models. Indeed, using Lyapunov approach, we prove that, if the control reproduction number \mathcal{R}_c is less than one, then the disease-free equilibrium point of both models is globally asymptotically stable under certain condition. We also prove that both models can admit at least one endemic equilibrium when $\mathcal{R}_c > 1$. The existence conditions of multiple positive equilibrium points are obtained in term of the vaccination coverage parameter. Using the Banach contraction principle, we prove the existence and the uniqueness of the solutions of each of the fractional models, follows by the global stability of the fractional model via the Ulam-Hyers method. To calibrate the model, we use reported cases of hepatitis B in Nigeria. We thus perform parameter estimations. We find that $\mathcal{R}_c \approx 1.766$, which means that the disease is endemic in this country since $\mathcal{R}_c > 1$. We then construct a numerical scheme using the Adams-Bashforth method, and finally perform numerical simulations, not only to validate the obtained theoretical results, but also to see how the model behaves when the fractional order parameter α varies between 0.6 and 1.

Key words: Hepatitis B virus, Imperfect vaccine, Caputo derivative, Asymptotic stability, Banach contraction principle, Ulam-Hyers stability, Adams-Bashforth scheme.

2000 MSC: 26A33, 34C60, 92C60, 92D30

1. Introduction

Hepatitis B is a liver infection caused by the Hepatitis B virus (HBV). The infection can be acute (severe and short-term) or chronic (long-term). It can also cause chronic infections and pose a significant risk of death from cirrhosis or liver cancer. Hepatitis B is most usually passed from mother to child at birth or via horizontal transmission, particularly between infected and uninfected children, during the first five years of life [1]. Hepatitis B virus can also be transferred by amputations, tattoos, piercings, and contact with infected blood or biological fluids such as saliva, menstrual fluids, vaginal secretions, or sex fluid. Approximately 1% of those living with HBV (2.7 million) are also infected with HIV. Inversely, the

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global prevalence of HBV infection among people infected with VIH is 7.4%. Since 2015, the OMS has recommended treating every subject diagnosed with VIH regardless of the stage of the disease. Tenofovir, which is included in the therapeutic combinations recommended for the first-line treatment of HIV infections, is also effective against HBV [2, 3].

Since Bernoulli's work in 1760 to assess the efficacy of varioalation, a crude type of smallpox vaccination [4], and Sir Ronald Ross on malaria [5], mathematical modeling has been an important tool in the description, follow-up, forecasting, and control of infectious illnesses (see for example [6, 7, 8, 9, 10, 11, 12, 13, 14] and the references therein). With regard to the transmission dynamics of HBV, the first models were formulated by Edmunds *et al.* [15]. They developed a mathematical model based on compartmental modelling to characterize the transmission dynamics of the hepatitis B virus (HBV) in a high-endemic nation (Gambia). Their model incorporates all three major transmission routes: perinatal, horizontal, and sexual transmission. The model also accounts for the demographics of a typical developing country, including age-dependence in transmission rates and the likelihood of becoming a chronic carrier. Through numerical simulations, they found that eradicating HBV may be achieved by immunizing less than 70% of infants, a relatively low rate compared to most childhood viral infections. In [16], Williams *et al.* formulated a model to evaluate and compare effectiveness of different immunization policies in United Kingdom (UK). Several works are done in the same year in this sense (see for example [17, 18]). Since then, several models have emerged [19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29]. In [22], the authors developed a novel mathematical model to better understand the dynamics of the Hepatitis B virus (HBV) in asymptomatic carriers and various vaccination classes. The problem was initially defined in integer order derivative and then extended using the fractional operator due to its benefits. They meticulously investigate the model's local and global asymptotic analysis in integer order. When $R_0 < 1$, the model is asymptotically stable both locally and globally. The fractional order model is defined, along with its existence and uniqueness. In order to graphically assess the fractional order model solution, they performed more comprehensive numerical findings for the factors that have a significant impact on disease eliminations using a useful numerical approach called the Mittag-Leffler approach.

In [22], the authors believe that vaccination is perfect, meaning that vaccine efficacy is 100 percent. Despite the World Health Organization's recommendation for a vaccination program for infants in areas with a high prevalence, hepatitis B remains a significant public health issue in Sub-Saharan African nations such as Cameroon and Nigeria. As a result, assuming vaccine efficacy to be flawless may bias prediction outcomes. Furthermore, the force of infection is dependent on the law of mass action, which is expressed as $f(I) = \beta I$. This means that the number of healthy persons decreases in proportion to the number of previously infected individuals and those who have not yet been affected. To improve this model, we reformulate a new model in which we consider that: (i) vaccine efficacy is not 100%; (ii) A fraction of carrier individuals received a treatment can acquired a definitive immunity, and the other fraction can take the vaccine; (iii) The force of infection depends of the density (standard incidence). We begin by providing some important definitions and results for fractional calculus. We then formulate the novel model, and then compute the control reproduction number \mathcal{R}_c , and prove the local and global asymptotic stability under condition of the hepatitis B-free equilibrium point whenever $\mathcal{R}_c < 1$. If the condition is violated, we find that the model can exhibits a backward bifurcation phenomenon. We also prove existence of at least one endemic equilibrium when $\mathcal{R}_c > 1$. The existence and uniqueness, as well as global stability of solution of the fractional model are proved based on

the Banach contraction principle, and Ulam-Hyers criterion, respectively. Using real data of Nigeria, we calibrate the model by performing parameter estimation, and thus estimated the value of \mathcal{R}_c . We construct a numerical scheme based on the Adams-Bashforth method, and finally perform several numerical simulations to not only to validate the obtained theoretical results, but also to see how the model behaves when the fractional order parameter α varies.

The rest of the work are structured as follows: Section 2 is devoted to preliminary definitions and results. The new HBV transmission model is formulated in Section 3. Theoretical results are done in Section 4. Model calibration, disease prediction, and numerical simulations are done in Section 5. A conclusion round up the work.

2. Preliminary definitions and results

In this section, we give some useful definitions and results concerning fractional calculus.

Definition 1 (The R-L integral). *Let $f \in L^1([0; a], \mathbb{R}_+)$, $a > 0$. The fractional order integral of f of order $\alpha > 0$, in the sense of Riemann-Liouville, is defined as*

$${}_a^C \mathcal{I}_t^\alpha (f(t)) = \frac{1}{\Gamma(\alpha)} \int_0^t f(\theta)(t - \theta)^{\alpha-1} d\theta. \quad (1)$$

Definition 2 (The Caputo derivative [30]). *Let $f \in \mathcal{C}^m([0; a])$, $a > 0$, $\alpha \in \mathbb{R}$, $m \in \mathbb{N}$ such that $m - 1 < \alpha < m$. The Caputo fractional order derivative of f of order φ is defined as*

$${}_a^C \mathbb{D}_t^\varphi (f(t)) = \frac{1}{\Gamma(\alpha - m)} \int_a^t (t - \theta)^{m-\alpha-1} f^{(m)}(\theta) d\theta, \quad t > 0. \quad (2)$$

Definition 3 (The Mittag-Leffler function [31]). *The Mittag-Leffler function of order $\alpha > 0$ is an entire function defined by the series*

$$\mathbf{E}_\alpha(x) = \sum_{k=0}^{\infty} \frac{x^k}{\Gamma(\alpha k + 1)}. \quad (3)$$

The following relation is valid

$${}_a^C \mathcal{I}_t^\varphi [{}_a^C \mathbb{D}_t^\varphi (f(t))] = f(t) - f(a). \quad (4)$$

3. Model formulations and basic results

In [32], Li et al. formulated and studied a extended SVEIR hepatitis B model with asymptomatic carriers and vaccination process. Indeed, they divided the traditional I class into three (03) infectious classes namely I_a for acute infected individuals with symptoms, I_{ac} for asymptomatic carrier individuals, and I_c for carrier individuals. The authors considered that vaccination is perfect. Perfect vaccine implies that all vaccinated individuals do not contract the hepatitis B virus. Since immunity acquired by vaccine greatly depends on the immune status of each person, this assumption is not realistic. They suppose that carrier individuals receive vaccine and do not recovered to the infection. They also suppose that transmission process consist to a mass action law. In the present work, we reformulated this model by including two principal assumptions:

1. Imperfect vaccine which means that a fraction of susceptible individuals who have vaccinated can be infected;

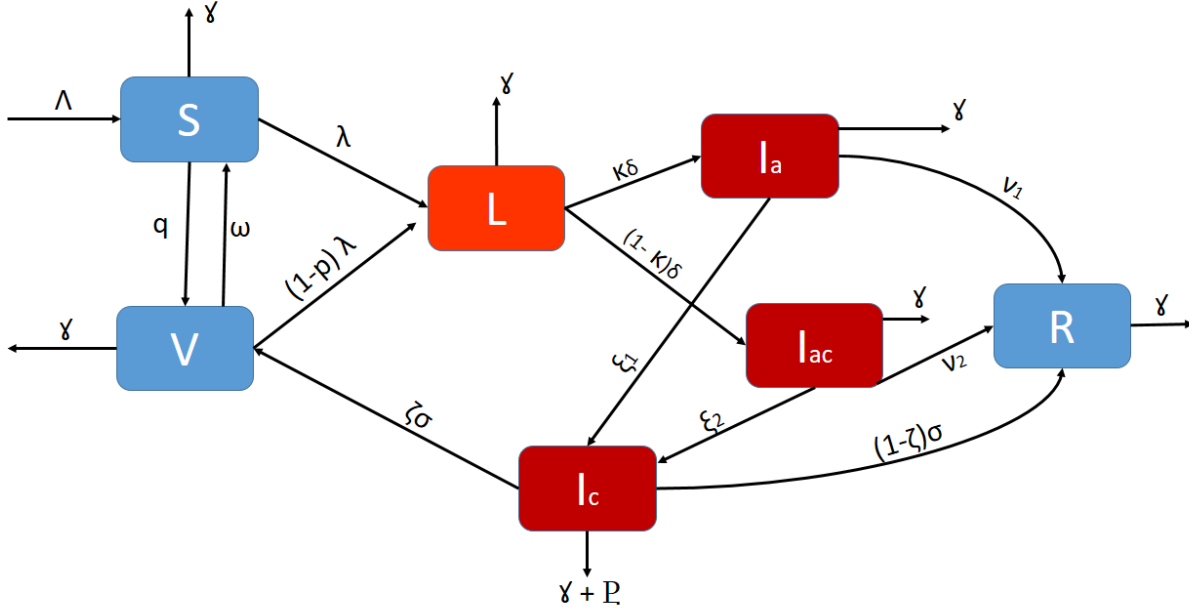


Figure 1: Schematic of the Hepatitis B virus transmission dynamics.

2. Carrier individuals can received a treatment, which means that a fraction of carrier individuals can acquired a definitive immunity, and the other fraction can take the vaccine;
3. The standard incidence function traduce the infection law.

Taking into account these three assumptions, the schematic compartmental diagram of the HBV model is depicted in Figure 1. The corresponding equations of each state variables putted together give the following system:

$$\left\{ \begin{array}{l}
 \mathbb{D}_t^\alpha S(t) = \Lambda + \omega V(t) - \lambda S(t) - \overbrace{(\gamma + \gamma)}^{k_1} S(t), \\
 \mathbb{D}_t^\alpha V(t) = qS(t) + \zeta\sigma I_c(t) - (1-p)\lambda(t)V(t) - \overbrace{(\omega + \gamma)}^{k_2} V(t), \\
 \mathbb{D}_t^\alpha L(t) = \lambda [S(t) + (1-p)V(t)] - \overbrace{(\gamma + \delta)}^{k_3} L(t), \\
 \mathbb{D}_t^\alpha I_a(t) = \delta\kappa L(t) - \overbrace{(\gamma + \nu_1 + \xi_1)}^{k_4} I_a(t), \\
 \mathbb{D}_t^\alpha I_{ac}(t) = \delta(1-\kappa)L(t) - \overbrace{(\gamma + \nu_2 + \xi_2)}^{k_5} I_{ac}(t), \\
 \mathbb{D}_t^\alpha I_c(t) = \xi_1 I_a(t) + \xi_2 I_{ac}(t) - \overbrace{(\gamma + \varrho + \sigma)}^{k_6} I_c(t), \\
 \mathbb{D}_t^\alpha R(t) = \nu_1 I_a(t) + \nu_2 I_{ac}(t) + (1-\zeta)\sigma I_c(t) - \gamma R(t).
 \end{array} \right. \quad (5)$$

In system (5), \mathbb{D}_t^α stands for the differential operator with respect of time t and of order $0 < \alpha \leq 1$; S , V , L , I_a , I_{ac} , I_c , and R denote susceptible individuals, vaccinated individuals, Infected individuals in latent period, acute infected individuals with symptoms, asymptomatic individuals, carrier individuals, and recovered individuals, respectively. Λ is

the recruitment rate, q denoted the vaccination rate, ω is the vaccine waning rate, p is the vaccine efficacy, γ denoted the natural death rate, σ is the recovered rate of carrier individuals, $1/\delta$ denotes the latent time period, ξ_1 is the rate of acute symptomatic individuals who become carriers while ξ_2 is the the rate of asymptomatic individuals who become carriers, ν_1 (resp. ν_2) is the rate of acute symptomatic individuals (resp. asymptomatic individuals) who recovered to the infection. ζ and κ are rates while τ_1 and τ_2 are modification parameters which represent the infectiousness of acute infected individuals with symptoms and asymptomatic individuals, respectively. Susceptible individuals or vaccinated individuals can acquired the infection through a direct contact with either acute infected individuals with symptoms, asymptomatic individuals or carrier individuals. The infection force (FOI) is given by

$$\lambda(t) = \beta \frac{(I_a(t) + \tau_1 I_{ac}(t) + \tau_2 I_c(t))}{N(t)}, \quad (6)$$

where β is the transmission rate, and $N(t)$ denotes the total population at time $t \geq 0$. Thus $N(t) = S(t) + V(t) + L(t) + I_a(t) + I_{ac}(t) + I_c(t) + R(t)$.

The schematic illustration of the model (5) is depicted in Figure 1.

We set $\mathbf{x} = (S, V, L, I_a, I_{ac}, I_c, R)'$ the vector of state variables and

$$\mathbb{R}_+^7 = \{\mathbf{x} \in \mathbb{R}^7 : \mathbf{x}_i \geq 0, i \in [1; 7] \cap \mathbb{N}\}.$$

System (5) can rewritten in the following compact form

$$\begin{cases} \frac{d\mathbf{x}}{dt} = \mathbf{F}(t, \mathbf{x}) = (\mathbf{F}_1(\mathbf{x}), \mathbf{F}_2(\mathbf{x}), \dots, \mathbf{F}_7(\mathbf{x}))', \\ \mathbf{x}(t_0) = \mathbf{x}_0 = (S_0, V_0, L_0, I_{a0}, I_{ac0}, I_{c0}, R_0)' \in \mathbb{R}_+^7, \end{cases} \quad (7)$$

where $\mathbf{F} : \mathbb{R}^7 \rightarrow \mathbb{R}^7$ represents the right hand-side of (5), and $(\bullet)'$ stands for the transposition operator. According to [33, Theorem III.10.VI], for $x(0) \in \mathbb{R}_+^7$, a unique solution of (5) exists, at least locally, and remains in \mathbb{R}_+^7 for its maximal interval of existence [33, Theorem III.10.XVI]. Hence model (5) is biologically well-defined.

We first prove that the each state variables of the model is nonnegative and bounded. We thus claim the following result:

Lemma 1 (Positivity). *Each solution $x(T)$ of (5) with nonnegative initial conditions $X(0)$, is nonnegative for all time $t \geq 0$.*

Proof. Following the proof of Theorem 2.2 in [34], from (5), we have

$$\begin{cases} \mathbb{D}_t^\alpha S(t)|_{S=0} & = \Lambda > 0, \\ \mathbb{D}_t^\alpha V(t)|_{V=0, S \geq 0, I_c \geq 0} & = qS(t) + \sigma\zeta I_c(t) \geq 0, \\ \mathbb{D}_t^\alpha L(t)|_{S, V, I_a, I_{ac}, I_c \geq 0, L=0} & = \lambda(t) [S(t) + (1-p)V(t)] \geq 0, \\ \mathbb{D}_t^\alpha I_a(t)|_{L \geq 0, I_a=0} & = \delta\kappa L(t) \geq 0, \\ \mathbb{D}_t^\alpha I_{ac}(t)|_{I_{ac}=0, L \geq 0} & = \delta(1-\kappa)L(t), \\ \mathbb{D}_t^\alpha I_c(t)|_{I_a, I_{ac} \geq 0, I_c=0} & = \xi_1 I_a(t) + \xi_2 I_{ac}(t) \geq 0, \\ \mathbb{D}_t^\alpha R(t)|_{I_a, I_{ac}, I_c \geq 0, R=0} & = \nu_1 I_a(t) + \nu_2 I_{ac}(t) + (1-\zeta)\sigma I_c(t). \end{cases} \quad (8)$$

Thus, the Barrier theorem [35] allows for the nonnegativity of state variables of (5) to be obtained. Thus for system (5), the positive orthant of \mathbb{R}^7 is invariant. \square

Using the same argument as in [34, 32], it follows that model (5) is define in the following bounded and absorbed set

$$\Sigma = \left\{ (S, V, L, I_a, I_{ac}, I_c, R)' \in \mathbb{R}_+^7 : N := S + V + L + I_a + I_{ac} + I_c + R \leq \frac{\Lambda}{\gamma} \right\}, \quad (9)$$

in which system (5) define a dynamical system.

Lemma 2 (Boundedness). *The set $\Sigma \subset \mathbb{R}_+^7$ is attracting for Ebola model (5).*

Proof. Adding the equations of (5) together, permits to have

$$\mathbb{D}_t^\alpha N(t) = \Lambda - \gamma N(t) - \rho I_c(t) \leq \Delta - \gamma N(T).$$

The resolution of this equality yields $0 \leq N(t) \leq \frac{\Lambda}{\gamma} + \left(N(0) - \frac{\Lambda}{\gamma} \right) e^{-\gamma t}$, $\forall t \geq 0$, which implies that

$$\limsup_{t \rightarrow \infty} N(t) \leq \frac{\Lambda}{\gamma}.$$

Thus, Σ is attracting for (5). □

Since the state variable R doesn't appear in the rest of equations, model system (5) can be reduce to the following equivalent system

$$\begin{cases} \mathbb{D}_t^\alpha S(t) &= \Lambda + \omega V(t) - \lambda S(t) - k_1 S(t), \\ \mathbb{D}_t^\alpha V(t) &= qS(t) + \zeta \sigma I_c(t) - (1-p)\lambda(t)V(t) - k_2 V(t), \\ \mathbb{D}_t^\alpha L(t) &= \lambda [S(t) + (1-p)V(t)] - k_3 L(t), \\ \mathbb{D}_t^\alpha I_a(t) &= \delta \kappa L(t) - k_4 I_a(t), \\ \mathbb{D}_t^\alpha I_{ac}(t) &= \delta(1-\kappa)L(t) - k_5 I_{ac}(t), \\ \mathbb{D}_t^\alpha I_c(t) &= \xi_1 I_a(t) + \xi_2 I_{ac}(t) - k_6 I_c(t). \end{cases} \quad (10)$$

4. Mathematical analysis

4.1. The ODE-model

In this sub-section, we consider that the fractional order $\alpha = 1$, that is $\mathbb{D}_t^\alpha \equiv \frac{d}{dt}$. Thus the fractional-order model (10) matches with the following integer model

$$\begin{cases} \frac{d}{dt} S(t) &= \Lambda + \omega V(t) - \lambda(t)S(t) - k_1 S(t), \\ \frac{d}{dt} V(t) &= qS(t) + \sigma \zeta I_c(t) - (1-p)\lambda(t)V(t) - k_2 V(t), \\ \frac{d}{dt} L(t) &= \lambda(t) [S(t) + (1-p)V(t)] - k_3 L(t), \\ \frac{d}{dt} I_a(t) &= \delta \kappa L(t) - k_4 I_a(t), \\ \frac{d}{dt} I_{ac}(t) &= \delta(1-\kappa)L(t) - k_5 I_{ac}(t), \\ \frac{d}{dt} I_c(t) &= \xi_1 I_a(t) + \xi_2 I_{ac}(t) - k_6 I_c(t), \end{cases} \quad (11)$$

where $\lambda(t)$ is given by Eq. (6).

4.1.1. The disease-free equilibrium

The disease-free equilibrium of the model. (11) is given by $\mathcal{E}_0 = (S_0, V_0, 0, 0, 0, 0)'$ where $S_0 = \frac{k_2\Lambda}{\gamma(q+k_2)}$ and $V_0 = \frac{q\Lambda}{\gamma(q+k_2)}$. Using the next generation approach described in [36] by Van den Driessche and Watmough, we obtain the following matrices

$$F = \begin{pmatrix} 0 & \beta \frac{S_0+(1-p)V_0}{N_0} & \beta\tau_1 \frac{S_0+(1-p)V_0}{N_0} & \beta\tau_2 \frac{S_0+(1-p)V_0}{N_0} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad (12)$$

$$W = \begin{pmatrix} k_3 & 0 & 0 & 0 \\ -\delta\kappa & k_4 & 0 & 0 \\ -\delta(1-\kappa) & 0 & k_5 & 0 \\ 0 & -\xi_1 & -\xi_2 & k_6 \end{pmatrix}.$$

The next generation matrix is given by

$$NGM := FW^{-1} = \begin{pmatrix} \mathcal{R}_1 + \mathcal{R}_2 + \mathcal{R}_3 & \mathcal{A} & \mathcal{B} & \mathcal{C} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad (13)$$

where $\mathcal{R}_1 = \frac{\tau_2\beta\delta(\xi_1k_5\kappa + \kappa_1\xi_2k_4)(p_1q+k_2)}{k_3k_4k_5k_6(q+k_2)}$, $\mathcal{R}_2 = \frac{\beta\delta\kappa(p_1q+k_2)}{k_3k_4(q+k_2)}$, $\mathcal{R}_3 = \frac{\kappa_1\tau_1\beta\delta(p_1q+k_2)}{k_3k_5(q+k_2)}$, $\mathcal{A} = \frac{(k_6 + \xi_1\tau_2)\beta(p_1q+k_2)}{k_4k_6(q+k_2)}$, $\mathcal{B} = \frac{(\tau_1k_6 + \tau_2\xi_2)\beta(p_1q+k_2)}{k_5k_6(q+k_2)}$, and $\mathcal{C} = \frac{(p_1q+k_2)\tau_2\beta}{k_6(q+k_2)}$ with $p_1 = 1-p$ and $\kappa_1 = 1-\kappa$.

We finally obtain that the control reproduction number is equal to the spectral radius of the matrix NGM, as follow

$$\mathcal{R}_c := \rho(NGM) = \mathcal{R}_1 + \mathcal{R}_2 + \mathcal{R}_3. \quad (14)$$

The following result is a direct consequence of [36, Theorem 2].

Lemma 3. *The disease-free equilibrium \mathcal{E}_0 is locally asymptotically stable in Σ whenever $\mathcal{R}_c < 1$ and unstable otherwise.*

To prove the global stability of the DFE, we will use Theorem 2.1 in [37]. To this aim, by considering only infected compartments of system (10), we obtain

$$\mathbb{D}_t^\alpha \begin{pmatrix} L(t) \\ I_a(t) \\ I_{ac}(t) \\ I_c(t) \end{pmatrix} = (F - W) \begin{pmatrix} L(t) \\ I_a(t) \\ I_{ac}(t) \\ I_c(t) \end{pmatrix} - \mathcal{M}(S(t), V(t), L(t), I_a(t), I_{ac}(t), I_c(t)), \quad (15)$$

where F and W are the same matrices used to compute the control reproduction number (see Eq. (38)), and

$$\mathcal{M}(S(t), V(t), L(t), I_a(t), I_{ac}(t), I_c(t)) = \begin{pmatrix} \beta(I_a(t) + \tau_1 I_{ac}(t) + \tau_2 I_c(t)) \left(\frac{S_0 + (1-p)V_0}{N_0} - \frac{S(t) + (1-p)V(t)}{N(t)} \right) \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

Then, it follows that $\mathcal{M}(S(t), V(t), L(t), I_a(t), I_{ac}(t), I_c(t)) \geq \mathbf{0}_{\mathbb{R}^6}$ if the following condition $\frac{S_0 + (1-p)V_0}{N_0} \geq \frac{S(t) + (1-p)V(t)}{N(t)}$ is satisfied in Σ , for all $t > 0$. This means that

$$\mathbb{D}_t^\alpha \begin{pmatrix} L(t) \\ I_a(t) \\ I_{ac}(t) \\ I_c(t) \end{pmatrix} \leq (F - W) \begin{pmatrix} L(t) \\ I_a(t) \\ I_{ac}(t) \\ I_c(t) \end{pmatrix}.$$

Note that

$$W^{-1} = \begin{pmatrix} \frac{1}{k_3} & 0 & 0 & 0 \\ \frac{\delta \kappa}{k_3 k_4} & \frac{1}{k_4} & 0 & 0 \\ \frac{\delta(1-\kappa)}{k_3 k_5} & 0 & \frac{1}{k_5} & 0 \\ \frac{\xi_1 k_5 \delta \kappa + \xi_2 k_4 \delta(1-\kappa)}{k_3 k_4 k_5 k_6} & \frac{\xi_1}{k_4 k_6} & \frac{\xi_2}{k_5 k_6} & \frac{1}{k_6} \end{pmatrix} \geq \mathbf{0}_{\mathbb{R}^{4 \times 4}}.$$

We also have, from (12), that $F \geq 0$. Thus, from [37, Theorem 2.1], there exists a Lyapunov function for system (10) expressed as $\mathcal{K}(S, V, L, I_a, I_{ac}, I_c) = w'W^{-1}(L, I_a, I_{ac}, I_c)'$ where w' is the left eigenvector of the nonnegative matrix $W^{-1}Z$ corresponding to the eigenvalue \mathcal{R}_c . This implies that,

$$\mathbb{D}_t^\alpha \mathcal{K} = (\mathcal{R}_c - 1) w'(L, I_a, I_{ac}, I_c) - w'W^{-1}\mathcal{M}(S, V, L, I_a, I_{ac}, I_c) \leq 0.$$

Since $\mathcal{M}(S, V, L, I_a, I_{ac}, I_c) \geq \mathbf{0}_{\mathbb{R}^4}$, it follows that $\mathbb{D}_t^\alpha \mathcal{K} < 0$ whenever $\mathcal{R}_c < 1$, with $\mathbb{D}_t^\alpha \mathcal{K} = 0$ if and only if $(L, I_a, I_{ac}, I_c) = \mathbf{0}_{\mathbb{R}^4}$. It follows that the largest invariant set contained in $\{(S, V, L, I_a, I_{ac}, I_c) \in \mathbb{R}_+^6 : \mathbb{D}_t^\alpha \mathcal{K} = 0\}$ is $\{\mathcal{E}_0\}$. Thus, from LaSalle Invariance Principle [38], every solution of (10) with initials conditions in Σ converge to \mathcal{E}_0 when $t \rightarrow +\infty$. That is $(L, I_a, I_{ac}, I_c) \rightarrow (0, 0, 0, 0)$, $S \rightarrow S_0$ and $V \rightarrow V_0$ when $t \rightarrow +\infty$, which is equivalent to $(S, V, L, I_a, I_{ac}, I_c) \rightarrow (S_0, V_0, 0, 0, 0, 0)$ when $t \rightarrow +\infty$. Thus, the disease-free equilibrium \mathcal{E}_0 is globally asymptotically stable in Σ whenever $\mathcal{R}_c < 1$. The above analysis can be resume as follows:

Theorem 1. *If $\mathcal{R}_c < 1$, then the HBV-free equilibrium \mathcal{E}_0 is globally asymptotically stable in Σ provided*

$$\frac{S_0 + (1-p)V_0}{N_0} \geq \frac{S(t) + (1-p)V(t)}{N(t)}, \text{ for all } t > 0. \quad (16)$$

4.1.2. The Endemic equilibrium points

Let us represent by $\mathcal{E} = (S^*, V^*, L^*, I_a^*, I_{ac}^*, I_c^*)'$ a non-negative equilibrium point of system (11). Setting the right-hand sides of system (11) equal to zero, and solving each equation in term of λ^* gives

$$\begin{aligned} S^* &= \frac{(p_1 \lambda^* + k_2)\Lambda + \omega \sigma \zeta I_c^*}{k_2 \lambda^* + \gamma(q + k_2)}, V^* = \frac{qS^* + \sigma \zeta I_c^*}{k_2}, L^* = \frac{(S^* + p_1 V^*) \lambda^*}{k_3}, I_a^* = \frac{\delta \kappa}{k_4} L^*, \\ I_{ac} &= \frac{\delta \kappa_1}{k_5} L^*, I_c = \frac{\xi_2 I_{ac}^* + \xi_1 I_a^*}{k_6}, \end{aligned} \quad (17)$$

where λ^* is any non-negative solution of the following equation

$$\lambda^* [a(\lambda^*)^3 + b(\lambda^*)^2 + c\lambda^* + d] = 0, \quad (18)$$

with

$$\begin{aligned}
a &= p_1^2 \delta (\xi_1 k_5 \kappa + \kappa_1 \xi_2 k_4) \sigma \zeta, \\
b &= p_1 k_2 k_3 k_4 k_5 k_6 \left[\underbrace{\frac{\varrho \delta (\xi_1 k_5 \kappa + \kappa_1 \xi_2 k_4) (p_1 q + k_2)}{k_2 k_3 k_4 k_5 k_6}}_{\mathcal{R}_T} - 1 \right], \\
c &= (q + k_2) p_1 \gamma \left[\frac{a}{p_1^2} + k_3 k_4 k_5 k_6 \mathcal{R}_c \right] + [p_1 q + k_2] \frac{a}{p_1^2 \sigma \zeta} (\sigma \zeta \omega + k_2 \varrho), \\
d &= k_2 k_3 k_4 k_5 k_6 (q + k_2) \gamma (\mathcal{R}_c - 1),
\end{aligned}$$

and $p_1 = 1 - p$, $\kappa_1 = 1 - \kappa$.

Note that $\lambda^* = 0$ is a trivial solution of Eq. (18) which correspond to the disease-free equilibrium $\mathcal{E}_0 = (S^0, V^0, 0, 0, 0, 0)$. The rest of positive roots is obtained with the following equation

$$a(\lambda^*)^3 + b(\lambda^*)^2 + c\lambda^* + d = 0. \quad (19)$$

Coefficients a and c are always positive and coefficient d is positive (resp. negative) whenever \mathcal{R}_c is greater (resp. less) than one. Coefficient b is positive (resp. negative) whenever $\mathcal{R}_T > 1$ (resp. $\mathcal{R}_T < 1$).

Using the Descartes' rule of signs, we thus claim what follows.

Theorem 2. *Let us define*

$$\mathcal{R}_T = \frac{\varrho \delta (\xi_1 k_5 \kappa + \kappa_1 \xi_2 k_4) (p_1 q + k_2)}{k_2 k_3 k_4 k_5 k_6}. \quad (20)$$

The hepatitis B model (11) admits:

1. the disease-free equilibrium \mathcal{E}_0 which can coexist with one or three endemic equilibrium points whenever $\mathcal{R}_c < 1$;
2. the disease-free equilibrium \mathcal{E}_0 which can coexist with two endemic equilibrium points \mathcal{E}_1^- and \mathcal{E}_1^+ with $\mathcal{E}_1^- < \mathcal{E}_1^+$, whenever $\min(\mathcal{R}_c; \mathcal{R}_T) > 1$;
3. the disease-free equilibrium \mathcal{E}_0 which can coexist with two endemic equilibrium points \mathcal{E}_1^* and \mathcal{E}_2^* whenever $\mathcal{R}_c = 1$ and $\mathcal{R}_T < 1$;
4. No endemic equilibrium otherwise.

4.1.3. Effective bifurcation thresholds

In this section, we will determine the bifurcation thresholds of model (10), To this aim, we will express each condition of Theorem 2 in term of parameter q which is choose as bifurcation parameter, as follow:

Case 1 of Theorem 2 is equivalent to

$$q > q^* := \frac{k_2(\pi_2 - \pi_1)}{\pi_2 - p_1 \pi_1}, \quad (21)$$

where $\pi_1 = \beta \delta [\tau_2(\xi_1 k_5 \kappa + \kappa_1 k_4 \xi_2) + k_6(\kappa k_5 + \kappa_1 \tau_1 k_4)]$ and $\pi_2 = k_3 k_4 k_5 k_6$.

Case 2 of Theorem 2 is equivalent

$$q^\dagger < q < q^*, \quad (22)$$

where $q^\dagger := \frac{k_2 [\pi_2 - \varrho \delta (\xi_1 k_5 \kappa + \kappa_1 k_4 \xi_2)]}{p_1 \varrho \delta (\xi_1 k_5 \kappa + \kappa_1 k_4 \xi_2)}$.

Case 3 of Theorem 2 is equivalent to

$$q^* < q^\ddagger. \quad (23)$$

We thus claim the following result which is equivalent to Theorem 2.

Theorem 3. *The hepatitis model (24) has*

1. *the disease-free equilibrium \mathcal{E}_0 which can coexist with one or three endemic equilibrium points whenever condition (21) holds;*
2. *the disease-free equilibrium \mathcal{E}_0 which can coexist with two endemic equilibrium points \mathcal{E}_1^- and \mathcal{E}_1^+ with $\mathcal{E}_1^- < \mathcal{E}_1^+$, whenever condition (22) holds;*
3. *the disease-free equilibrium \mathcal{E}_0 which can coexist with two endemic equilibrium points \mathcal{E}_1^* and \mathcal{E}_2^* whenever condition (23);*
4. *No endemic equilibrium otherwise.*

4.2. The fractional model

Now, we consider that $0 < \alpha < 1$. For dimensional consistency emphasized by Diethelm in [39] (see also [40]), all model parameters except p and κ , have dimensions $\frac{1}{t^\alpha}$. Thus model (5) becomes

$$\left\{ \begin{array}{l} \mathbb{D}_t^\alpha S(t) = \Lambda^\alpha + \omega^\alpha V(t) - \lambda S(t) - \overbrace{(q^\alpha + \gamma^\alpha)}^{K_1} S(t), \\ \mathbb{D}_t^\alpha V(t) = q^\alpha S(t) + \zeta \sigma^\alpha I_c(t) - (1-p)\lambda(t)V(t) - \overbrace{(\omega^\alpha + \gamma^\alpha)}^{K_2} V(t), \\ \mathbb{D}_t^\alpha L(t) = \lambda [S(t) + (1-p)V(t)] - \overbrace{(\gamma^\alpha + \delta^\alpha)}^{K_3} L(t), \\ \mathbb{D}_t^\alpha I_a(t) = \delta^\alpha \kappa L(t) - \overbrace{(\gamma^\alpha + \nu_1^\alpha + \xi_1^\alpha)}^{K_4} I_a(t), \\ \mathbb{D}_t^\alpha I_{ac}(t) = \delta^\alpha (1-\kappa)L(t) - \overbrace{(\gamma^\alpha + \nu_2^\alpha + \xi_2^\alpha)}^{K_5} I_{ac}(t), \\ \mathbb{D}_t^\alpha I_c(t) = \xi_1^\alpha I_a(t) + \xi_2^\alpha I_{ac}(t) - \overbrace{(\gamma^\alpha + \varrho^\alpha + \sigma^\alpha)}^{K_6} I_c(t), \\ \mathbb{D}_t^\alpha R(t) = \nu_1 I_a(t) + \nu_2 I_{ac}(t) + (1-\zeta)\sigma I_c(t) - \gamma R(t) \end{array} \right. \quad (24)$$

where

$$\lambda(t) = \beta_1^\alpha \frac{I_a(t) + \tau_1 I_{ac}(t) + \tau_2 I_c(t)}{N(t)}. \quad (25)$$

System (24) is subject to the following initial conditions

$$\begin{aligned} S(0) &= S_0 > 0, V(0) = V_0 \geq 0, L(0) = L_0 \geq 0, \\ I_a(0) &= I_a^0 \geq 0, I_{ac}(0) = I_{ac}^0 \geq 0, I_c(0) = I_c^0 \geq 0. \end{aligned} \quad (26)$$

Let us set $x = (S, V, L, I_a, I_{ac}, I_c, R)'$ and $\mathcal{O}(t, x(t)) = (\phi_i)'$, $i \in [0, 7] \cap \mathbb{N}$, where ϕ_i for $i \in [0, 7] \cap \mathbb{N}$ are the right-hand side of system (24). Thus fractional model (24) is rewritten in the following compact form

$${}_a^C \mathbb{D}_t^\alpha x(t) = \mathcal{O}(t, x(t)), \quad x(0) = x_0 \geq 0, \quad t \in [0, a], \quad a > 0, \quad 0 < \alpha \leq 1. \quad (27)$$

The initial value problem (IVP) (27) is in turn rewritten in the following integral form

$$x(t) = x(0) + {}_a^C \mathcal{I}_t^\alpha (\mathbb{O}(t, x(t))). \quad (28)$$

Let us denote by $\Delta = \mathcal{C}([0; a], \mathbb{R})$ the Banach space of all continue functions from $[0; a]$ to \mathbb{R} . We endow Δ with the following norm

$$\|x(t)\|_\Delta = \sup_{t \in [0; a]} \{|x(t)|\},$$

where $|x(t)| = \sum_{i=1}^7 |x_i(t)|$, and $\forall i \in [0; 7] \cap \mathbb{N}$, $x_i(t) \in \Delta$. Let us consider the following operator $\mathcal{P} : \Delta \rightarrow \Delta$ defined by

$$(\mathcal{P}x)(t) = x(0) + {}_a^C \mathcal{I}_t^\alpha (\mathbb{K}(t, x(t))). \quad (29)$$

Due to the continuity of \mathbb{O} , the above operator is well-defined.

The following results hold. The proofs are obtained as the same ways than the results obtained for the model (5).

Theorem 4. *For $x(t) \geq \mathbf{0}_{\mathbb{R}^7}$, the solution $x(t)$ of the IVP (24) is positive whenever $t \geq 0$.*

Let us define the following subset of \mathbb{R}_+^7

$$\Sigma^\alpha = \left\{ x = (S, V, L, I_a, I_{ac}, I_c, R)' \in \mathbb{R}_+^7 : \left(\sum_{i=1}^7 x_i \right) \leq \frac{\Lambda^\alpha}{\gamma^\alpha} \right\}. \quad (30)$$

Theorem 5. *(Boundedness of solutions)*

The region Σ^α is positively invariant and attracting for system (24).

4.3. Existence and uniqueness of solutions

The following result is valid:

Lemma 4. *Let $\bar{x} = (\bar{S}, \bar{V}, \bar{L}, \bar{I}_a, \bar{I}_{ac}, \bar{I}_c, \bar{R})'$. The function $\mathbb{O} = (\mathbb{O}_i)'$ defined above satisfies $\|\mathbb{O}(t, x(t)) - \mathbb{O}(t, \bar{x}(t))\|_\Delta \leq \mathcal{N}_\mathbb{O} \|x - \bar{x}\|_\Delta$ for some $\mathcal{N}_\mathbb{O} > 0$.*

Proof. We proceed as follows for the first component of \mathbb{O} :

$$\begin{aligned} & |\mathbb{O}_1(t, x) - \mathbb{O}_1(t, \bar{x})| \\ & \leq K_1 |S - \bar{S}| + \omega^\alpha |V - \bar{V}| \\ & + \beta^\alpha \left| \frac{1}{\bar{N}\bar{N}} \right| \{ |SI_a\bar{N} - \bar{S}\bar{I}_a\bar{N}| + \tau_1 |SI_{ac}\bar{N} - \bar{S}\bar{I}_{ac}\bar{N}| + \tau_2 |SI_c\bar{N} - \bar{S}\bar{I}_c\bar{N}| \}, \\ & \leq K_1 |S(t) - \bar{S}(t)| + \omega^\alpha |V(t) - \bar{V}(t)| \\ & + \beta^\alpha \left| \frac{1}{\bar{N}\bar{N}} \right| \{ |\bar{N}I_a| |S - \bar{S}| + \bar{N}\bar{S} |I_a - \bar{I}_a| + \bar{I}_a\bar{S} |N - \bar{N}| \} \\ & + \beta^\alpha \left| \frac{1}{\bar{N}\bar{N}} \right| \{ \tau_1 [|\bar{N}I_{ac}| |S - \bar{S}| + \bar{N}\bar{S} |I_{ac} - \bar{I}_{ac}| + \bar{I}_{ac}\bar{S} |N - \bar{N}|] \} \\ & + \beta^\alpha \left| \frac{1}{\bar{N}\bar{N}} \right| \{ \tau_2 [|\bar{N}I_c| |S - \bar{S}| + \bar{N}\bar{S} |I_c - \bar{I}_c| + \bar{I}_c\bar{S} |N - \bar{N}|] \} \end{aligned} \quad (31)$$

After algebraic simplification of the right-hand side of the above inequality, we finally obtain

$$\begin{aligned}
& |\mathbb{O}_1(t, x) - \mathbb{O}_1(t, \bar{x})| \\
& \leq K_1 |S - \bar{S}| + \omega^\alpha |V - \bar{V}| + \beta^\alpha \left(\left| \frac{I_a}{N} \right| + \tau_1 \left| \frac{I_{ac}}{N} \right| + \tau_2 \left| \frac{I_c}{N} \right| \right) |S - \bar{S}| \\
& + \beta^\alpha \left| \frac{\bar{S}}{N} \right| |I_a - \bar{I}_a| + \beta^\alpha \tau_1 \left| \frac{\bar{S}}{N} \right| |I_{ac} - \bar{I}_{ac}| + \beta^\alpha \tau_2 \frac{\bar{S}}{N} |I_c - \bar{I}_c| + \beta^\alpha \left| \frac{\bar{I}_a \bar{S}}{N N} + \tau_1 \frac{\bar{I}_{ac} \bar{S}}{N N} + \tau_2 \frac{\bar{I}_c \bar{S}}{N N} \right| |N - \bar{N}| \\
& \leq \overbrace{\left[K_1 + \beta^\alpha (1 + \tau_1 + \tau_2) + \beta^\alpha (1 + \tau_1 + \tau_2) \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{11}} |S - \bar{S}| + \overbrace{\left[\omega^\alpha + \beta^\alpha (1 + \tau_1 + \tau_2) \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{12}} |V - \bar{V}| \\
& + \overbrace{\left[\beta^\alpha (1 + \tau_1 + \tau_2) \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{13}} |L - \bar{L}| + \overbrace{\left[\beta^\alpha [2 + \tau_1 + \tau_2] \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{14}} |I_a - \bar{I}_a| + \overbrace{\left[\beta^\alpha [1 + 2\tau_1 + \tau_2] \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{15}} |I_{ac} - \bar{I}_{ac}| \\
& + \overbrace{\left[\beta^\alpha [1 + \tau_1 + 2\tau_2] \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{16}} |I_c - \bar{I}_c| + \overbrace{\left[\beta^\alpha (1 + \tau_1 + \tau_2) \left| \frac{\bar{S}}{N} \right| \right]}^{\xi_{13}} |R - \bar{R}| \\
& \leq \mathbf{N}_1 (|S - \bar{S}| + |V - \bar{V}| + |L - \bar{L}| + |I_a - \bar{I}_a| + |I_{ac} - \bar{I}_{ac}| + |I_c - \bar{I}_c| + |R - \bar{R}|), \tag{32}
\end{aligned}$$

where $\mathbf{N}_1 = \max_{t \in [0, a]} \left\{ \sum_{i=1}^6 \xi_{1i} \right\}$.

Similarly, with \mathbb{O}_2 , we also have :

$$\begin{aligned}
|\mathbb{O}_2(t, x) - \mathbb{O}_2(t, \bar{x})| &= |q^\alpha(S - \bar{S}) - K_2(V - \bar{V}) + \xi\sigma^\alpha(I_c - \bar{I}_c) - p_1(\lambda V - \bar{\lambda}\bar{V})|, \\
&\leq q^\alpha |S - \bar{S}| + K_2 |V - \bar{V}| + \xi\sigma^\alpha |I_c - \bar{I}_c| + p_1 |\lambda V - \bar{\lambda}\bar{V}|, \\
&\leq q^\alpha |S - \bar{S}| + K_2 |V - \bar{V}| + \xi\sigma^\alpha |I_c - \bar{I}_c| \\
&\quad + p_1\beta^\alpha \left| \frac{I_a}{N} \right| |S - \bar{S}| + p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| |I_a - \bar{I}_a| + p_1\beta^\alpha \left| \frac{\bar{I}_a\bar{V}}{N\bar{N}} \right| |N - \bar{N}|, \\
&\quad + p_1\beta^\alpha\tau_1 \left| \frac{I_{ac}}{N} \right| |S - \bar{S}| + p_1\beta^\alpha\tau_1 \left| \frac{\bar{V}}{N} \right| |I_{ac} - \bar{I}_{ac}| + p_1\beta^\alpha\tau_1 \left| \frac{\bar{I}_{ac}\bar{V}}{N\bar{N}} \right| |N - \bar{N}|, \\
&\quad + p_1\beta^\alpha\tau_2 \left| \frac{I_c}{N} \right| |S - \bar{S}| + p_1\beta^\alpha\tau_2 \left| \frac{\bar{V}}{N} \right| |I_c - \bar{I}_c| + p_1\beta^\alpha\tau_2 \left| \frac{\bar{I}_c\bar{V}}{N\bar{N}} \right| |N - \bar{N}|, \\
&\leq \overbrace{\left[q^\alpha + p_1\beta^\alpha \left| \frac{I_a}{N} \right| + p_1\beta^\alpha\tau_1 \left| \frac{I_{ac}}{N} \right| + p_1\beta^\alpha\tau_2 \left| \frac{I_c}{N} \right| + p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| [1 + \tau_1 + \tau_2] \right]}^{\xi_{21}} |S - \bar{S}| \\
&\quad + \overbrace{\left[K_2 + p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| [1 + \tau_1 + \tau_2] \right]}^{\xi_{22}} |V - \bar{V}| + \overbrace{p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| [1 + \tau_1 + \tau_2]}^{\xi_{23}} |L - \bar{L}| \\
&\quad + \overbrace{p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| [2 + \tau_1 + \tau_2]}^{\xi_{24}} |I_a - \bar{I}_a| + \overbrace{p_1\beta^\alpha [1 + 2\tau_1 + \tau_2] \left| \frac{\bar{V}}{N} \right|}^{\xi_{25}} |I_{ac} - \bar{I}_{ac}|, \\
&\quad + \overbrace{\left[\xi\sigma^\alpha + p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| (1 + \tau_1 + 2\tau_2) \right]}^{\xi_{26}} |I_c - \bar{I}_c| + \overbrace{p_1\beta^\alpha \left| \frac{\bar{V}}{N} \right| [1 + \tau_1 + \tau_2]}^{\xi_{23}} |R - \bar{R}|, \\
&\leq \mathbf{N}_2 (|S - \bar{S}| + |V - \bar{V}| + |L - \bar{L}| + |I_a - \bar{I}_a| + |I_{ac} - \bar{I}_{ac}| + |I_c - \bar{I}_c| + |R - \bar{R}|), \\
\end{aligned} \tag{33}$$

where $\mathbf{N}_2 = \max_{t \in [0, a]} \left\{ \sum_{i=1}^6 \xi_{2i} \right\}$.

$$\begin{aligned}
& |\mathbb{O}_3(t, x) - \mathbb{O}_3(t, \bar{x})| = |K_3(L - \bar{L}) + \lambda(S + p_1V) - \bar{\lambda}(\bar{S} + p_1\bar{V})|, \\
& \leq K_3 |L - \bar{L}| + |\lambda S - \bar{\lambda}\bar{S}| + p_1 |\lambda V - \bar{\lambda}\bar{V}|, \\
& \leq \overbrace{\left\{ \beta^\alpha (1 + \tau_1 + \tau_2) \left(1 + \left| \frac{\bar{S}}{N} \right| \right) + p_1 \beta^\alpha (1 + \tau_1 + \tau_2) \left(1 + \left| \frac{\bar{V}}{N} \right| \right) \right\}}^{\xi_{31}} |S - \bar{S}| \\
& + \beta^\alpha (1 + \tau_1 + \tau_2) \overbrace{\left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right]}^{\xi_{32}} |V - \bar{V}| + \overbrace{\left\{ K_3 + \beta^\alpha (1 + \tau_1 + \tau_2) \left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right] \right\}}^{\xi_{33}} |L - \bar{L}| \\
& + \beta^\alpha (2 + \tau_1 + \tau_2) \overbrace{\left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right]}^{\xi_{34}} |I_a - \bar{I}_a| + \beta^\alpha (1 + 2\tau_1 + \tau_2) \overbrace{\left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right]}^{\xi_{35}} |I_{ac} - \bar{I}_{ac}| \\
& + \beta^\alpha (1 + \tau_1 + 2\tau_2) \overbrace{\left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right]}^{\xi_{36}} |I_c - \bar{I}_c| + \beta^\alpha (1 + \tau_1 + \tau_2) \overbrace{\left[\left| \frac{\bar{S}}{N} \right| + p_1 \left| \frac{\bar{V}}{N} \right| \right]}^{\xi_{32}} |R - \bar{R}| \\
& \leq \mathbf{N}_3 (|S - \bar{S}| + |V - \bar{V}| + |L - \bar{L}| + |I_a - \bar{I}_a| + |I_{ac} - \bar{I}_{ac}| + |I_c - \bar{I}_c| + |R - \bar{R}|), \tag{34}
\end{aligned}$$

where $\mathbf{N}_3 = \max_{t \in [0, a]} \left\{ \sum_{i=1}^6 \xi_{3i} \right\}$.

Based on the analogous reasoning, we obtain ξ_i , $i \in [4; 7] \cap \mathcal{N}$:

$$\begin{aligned}
& |\mathbb{O}_3(t, x) - \mathbb{O}_3(t, \bar{x})| \leq \mathbf{N}_4 (|L - \bar{L}| + |I_a - \bar{I}_a|), \\
& |\mathbb{O}_4(t, x) - \mathbb{O}_4(t, \bar{x})| \leq \mathbf{N}_5 (|L - \bar{L}| + |I_{ac} - \bar{I}_{ac}|), \\
& |\mathbb{O}_5(t, x) - \mathbb{O}_5(t, \bar{x})| \leq \mathbf{N}_6 (|I_a - \bar{I}_a| + |I_{ac} - \bar{I}_{ac}| + |I_c - \bar{I}_c|), \\
& |\mathbb{O}_6(t, x) - \mathbb{O}_6(t, \bar{x})| \leq \mathbf{N}_7 (|I_a - \bar{I}_a| + |I_{ac} - \bar{I}_{ac}| + |I_c - \bar{I}_c| + |R - \bar{R}|), \tag{35}
\end{aligned}$$

where $\mathbf{N}_4 = \delta^\alpha \kappa + K_4$, $\mathbf{N}_5 = \delta^\alpha \kappa_1 + K_5$, $\mathbf{N}_6 = \xi_1^\alpha + \xi_2^\alpha + K_6$, $\mathbf{N}_7 = \nu_1^\alpha + \nu_2^\alpha + (1 - \zeta)\sigma^\alpha + \gamma^\alpha$.

Therefore, we finally obtain

$$\begin{aligned}
\| \mathbb{O}(t, x) - \mathbb{O}(t, \bar{x}) \|_\Delta &= \sup_{t \in [0, a]} \sum_{i=1}^7 |\mathbb{O}_i(t, x) - \mathbb{O}_i(t, \bar{x})| \\
&\leq \overbrace{(\mathbf{N}_1 + \mathbf{N}_2 + \mathbf{N}_3 + \mathbf{N}_4 + \mathbf{N}_5 + \mathbf{N}_6 + \mathbf{N}_7)}^{\mathbf{N}_\eta} \| x - \bar{x} \|_\Delta.
\end{aligned}$$

□

Theorem 6. *Let the result of Lemma 4 hold and $\varpi = \frac{a^\alpha}{\Gamma(\alpha + 1)}$. If $\varpi \mathbf{N}_\eta < 1$, then there exists a unique solution of the model Equation (24) on $[0, a]$, which is uniformly Lyapunov-stable.*

Proof. The function $\mathbb{O} : [0, a] \times \mathbb{R}_+^7 \rightarrow \mathbb{R}^7$ is clearly continuous in its domain. Thus, the existence of the solutions of Equations (24) and (27) follows from (Theorem 3.1, [41]).

The Banach contraction mapping principle on operator \mathcal{P} (see Equation (29)) will be used in the following to prove the uniqueness of the solution of the fractional model Equation (24). By definition, $\sup_{t \in [0, a]} \|\mathbb{O}(t, 0)\| = \Lambda^\alpha$. Let us now define $\Pi > \frac{\|x_0\| + \varpi \Lambda^\alpha}{1 - \varpi \mathbf{N}_\Delta}$ and a closed convex set $\mathbf{Z}_\Pi = \{x \in \Delta : \|x\|_\eta \leq \Pi\}$. Thus, for the sel-map property, it suffices to show that $\mathcal{P}\mathbf{Z}_\Pi \subseteq \mathbf{Z}_\Pi$. Let $x \in \mathbf{Z}_\Pi$, we have

$$\begin{aligned}
\|\mathcal{P}x\|_\Delta &= \sup_{t \in [0, a]} \left\{ \left| x_0 + \frac{1}{\Gamma(\alpha)} \int_0^t (t - \epsilon)^{\alpha-1} \mathcal{O}(\epsilon, x(\epsilon)) d\epsilon \right| \right\}, \\
&\leq |x_0| + \frac{1}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} (|\mathbb{O}(\epsilon, x(\epsilon)) - \mathbb{O}(\epsilon, 0)| + |\mathbb{O}(\epsilon, 0)|) d\epsilon \right\}, \\
&\leq |x_0| + \frac{1}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} (\|\mathbb{O}(\epsilon, x(\epsilon)) - \mathbb{O}(\epsilon, 0)\|_\Delta + \|\mathbb{O}(\epsilon, 0)\|_\Delta) d\epsilon \right\}, \\
&\leq |x_0| + \frac{\mathbf{N}_\Delta \|x\|_\Delta + \Lambda^\alpha}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} d\epsilon \right\}, \\
&\leq |x_0| + \frac{\mathbf{N}_\Delta \Pi + \Lambda^\alpha}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} d\epsilon \right\}, \\
&= |x_0| + \frac{a^\alpha}{\Gamma(\alpha + 1)} (\mathbf{N}_\Delta \Pi + \Lambda^\alpha), \\
&= |x_0| + \varpi (\mathbf{N}_\Delta \Pi + \Lambda^\alpha), \\
&\leq \Pi.
\end{aligned}$$

□

Then, $\mathcal{P}x \subseteq \mathbf{Z}_\Pi$ and \mathcal{P} are indeed the self-map. It remains to show that \mathcal{P} is a contraction. Let \mathcal{X} and $\bar{\mathcal{X}}$ two solutions of Equation (27). Using the result of Lemma 4, we obtain

$$\begin{aligned}
\|\mathcal{P}x - \mathcal{P}\bar{x}\|_\Delta &= \sup_{t \in [0, a]} \{ |(\mathcal{P}x)(t) - (\mathcal{P}\bar{x})(t)| \}, \\
&= \frac{1}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} |\mathbb{O}(\epsilon, x(\epsilon)) - \mathbb{O}(\epsilon, \bar{x}(\epsilon))| d\epsilon \right\}, \\
&\leq \frac{\mathbf{N}_\Delta}{\Gamma(\alpha)} \sup_{t \in [0, a]} \left\{ \int_0^t (t - \epsilon)^{\alpha-1} (|x(\epsilon) - \bar{x}(\epsilon)|) d\epsilon \right\}, \\
&\leq \varpi \mathbf{N}_\Delta \|x - \bar{x}\|_\Delta.
\end{aligned}$$

The condition $\varpi \mathbf{N}_\Delta < 1$ ensures that \mathcal{P} is a contraction mapping. Thus, by the Banach contraction mapping principle, \mathcal{P} has a unique fixed point on $[0, a]$, which is the solution of Equation (24). Theorem 3.2 in [41] ensures the uniformly Lyapunov stability of the solution.

4.4. Global Stability of the Fractional Model

In what follows, we will perform the global stability of the fractional-order model Equation (24) in the sense of Ulam–Hyers [42, 43]. To this aim, we introduce the following inequality:

$$\left| {}_0^C \mathbb{D}^\alpha x(t) - \mathbb{O}(t, x(t)) \right| \leq b, \quad t \in [0; a]. \quad (36)$$

A function $\bar{x} \in \Delta$ is a solution of Equation (36) if there exists $\aleph \in \Delta$ satisfying

1. $|\aleph(t)| \leq b$;
2. ${}^C_0\mathbb{D}^\alpha \bar{x}(t) = \mathbb{O}(t, \bar{x}(t)) + \aleph(t)$, $t \in [0; a]$.

Since $\bar{x} \in \Delta$ is a solution of Equation (36), then $\bar{x} \in \Delta$ is also a solution of the following integral inequality

$$\left| \bar{x}(t) - \bar{x}(0) - \frac{1}{\Gamma(\alpha)} \int_0^t (t - \epsilon)^{\alpha-1} \mathbb{O}(\epsilon, \bar{x}(\epsilon)) d\epsilon \right| \leq \varpi b. \quad (37)$$

We claim the following result:

Theorem 7. *Assume that the result of Lemma 4 holds, and $1 - \varpi \mathbf{N}_\Delta > 0$ with $\varpi = \frac{a^\nu}{\Gamma(\alpha + 1)}$. The fractional order model Equation (27) (and equivalently Equation (24)) is Ulam–Hyers-stable and, consequently, generalized Ulam–Hyers-stable.*

Proof. Let x be a unique solution of Equation (27), and \bar{x} satisfies Equation (36). For $b > 0$, $t \in [0, a]$, we have

$$\begin{aligned} \|\bar{x}(t) - x(t)\|_\eta &= \sup_{t \in [0, a]} |\bar{x}(t) - x(t)| \\ &= \sup_{t \in [0, a]} \left| \bar{x}(t) - x(0) - \frac{1}{\Gamma(\alpha)} \int_0^t (t - \epsilon)^{\alpha-1} \mathbb{O}(\epsilon, x(\epsilon)) d\epsilon \right| \\ &\leq \sup_{t \in [0, a]} \left| \bar{x}(t) - \bar{x}(0) - \frac{1}{\Gamma(\alpha)} \int_0^t (t - \epsilon)^{\alpha-1} \mathbb{O}(\epsilon, \bar{x}(\epsilon)) d\epsilon \right| \\ &\quad + \sup_{t \in [0, a]} \frac{1}{\Gamma(\alpha)} \int_0^t (t - \epsilon)^{\alpha-1} |\mathbb{O}(\epsilon, \bar{x}(\epsilon)) - \mathbb{O}(\epsilon, x(\epsilon))| d\epsilon \\ &\leq \varpi b + \frac{\mathbf{N}_\Delta}{\Gamma(\alpha)} \sup_{t \in [0, a]} \int_0^t (t - \epsilon)^{\alpha-1} |\bar{x}(\epsilon) - x(\epsilon)| d\epsilon \\ &\leq \varpi b + \varpi \mathcal{N}_\Delta \|\bar{x}(t) - x(t)\|_\Delta, \end{aligned}$$

which implies that $\|\bar{x}(t) - x(t)\|_\Delta \leq b \overbrace{\left(\frac{\varpi}{1 - \varpi \mathbf{N}_\Delta} \right)}^{\mathbf{C}_\Delta}$. Thus, from (Definitions 4.5 & 4.6, [42]), we conclude that the fractional order model Equation (27) (and, equivalently, Equation (24)) is Ulam–Hyers-stable and, consequently, generalized Ulam–Hyers-stable. This ends the proof. \square

4.5. Asymptotic stability

As for the case of the model with integer derivative (10), fractional model (24) admits always one stationary point, also called disease-free equilibrium (DFE), $\mathcal{E}_0 = (S_0, V_0, 0, 0, 0, 0, 0)$ where $S_0 = \frac{K_2 \Lambda^\alpha}{\gamma^\alpha (q^\alpha + K_2)}$ and $V_0 = \frac{q^\alpha \Lambda^\alpha}{\gamma^\alpha (q^\alpha + K_2)}$.

As in the case of the ODE model (10), we compute the control reproduction number, denoted by \mathcal{R}_c using the next generation approach (see [44, 36]), and the control reproduction number of the fractional model (24) is given by

$$\mathcal{R}_c := \rho(\text{NGM}) = \mathcal{R}_1 + \mathcal{R}_2 + \mathcal{R}_3, \quad (38)$$

where $\mathcal{R}_1 = \frac{\tau_2^\alpha \beta^\alpha \delta^\alpha (\xi_1^\alpha K_5 \kappa + \kappa_1 \xi_2^\alpha K_4) (p_1 q^\alpha + K_2)}{K_3 K_4 K_5 K_6 (q^\alpha + K_2)}$, $\mathcal{R}_2 = \frac{\beta^\alpha \delta^\alpha \kappa (p_1 q^\alpha + K_2)}{K_3 K_4 (q^\alpha + K_2)}$,
 $\mathcal{R}_3 = \frac{\kappa_1 \tau_1^\alpha \beta^\alpha \delta^\alpha (p_1 q^\alpha + K_2)}{K_3 K_5 (q^\alpha + k_K 2)}$, with $p_1 = 1 - p$ and $\kappa_1 = 1 - \kappa$.

Before study the local stability of the disease-free equilibrium, let us recall the following result.

Lemma 5. [45, Theorem 4.4] *The disease-free equilibrium of the fractional model (24) is locally asymptotically stable if all the eigenvalues μ_i of its Jacobian matrix evaluated at the DFE satisfy $|\arg(\mu_i)| > \frac{\alpha\pi}{2}$, $i = [1; 7] \cap \mathbb{N}$.*

The Jacobian of system (24) evaluated at the disease-free equilibrium \mathcal{E}_0 is given by

$$J(\mathcal{E}_0) = \begin{pmatrix} -K_1 & \omega^\alpha & 0 & -\frac{S_0 \beta}{N_0} & -\frac{S_0 \tau_1 \beta}{N_0} & -\frac{S_0 \tau_2 \beta}{N_0} \\ q^\alpha & -K_2 & 0 & -\frac{V_0 p_1 \beta}{N_0} & -\frac{V_0 p_1 \tau_1 \beta}{N_0} & \sigma^2 \zeta - \frac{V_0 p_1 \tau_2 \beta}{N_0} \\ 0 & 0 & -K_3 & \frac{H_0 \beta}{N_0} & \frac{H_0 \tau_1 \beta}{N_0} & \frac{H_0 \tau_2 \beta}{N_0} \\ 0 & 0 & \delta^\alpha \kappa & -K_4 & 0 & 0 \\ 0 & 0 & \kappa_1 \delta^\alpha & 0 & -K_5 & 0 \\ 0 & 0 & 0 & \xi_1^\alpha & \xi_2^\alpha & -K_6 \end{pmatrix}.$$

The characteristic equation associated to $J(\mathcal{E}_0)$ is given by

$$\underbrace{[\mu^2 + (K_2 + K_1) \mu + \gamma^\alpha (q^\alpha + K_2)]}_{\Phi_1(\mu)} \underbrace{[A_4 \mu^4 + A_3 \mu^3 + A_2 \mu^2 + A_1 \mu + A_0]}_{\Phi_2(\mu)} = 0, \quad (39)$$

where

$$A_4 = (K_6 + \xi_1^\alpha \tau_2^\alpha) K_5 \kappa + (\tau_1^\alpha K_6 + \tau_2^\alpha \xi_2^\alpha) K_4 \kappa_1,$$

$$A_3 = (K_5 K_6^2 + \xi_1^\alpha \tau_2^\alpha (K_5 K_6 + K_5^2 + (K_4 + K_3) K_5) + (K_5^2 + (K_4 + K_3) K_5) K_6) \kappa \\ + \tau_1^\alpha (\kappa_1 K_4 K_6^2 + (\kappa_1 K_4 K_5 + \kappa_1 K_4^2 + \kappa_1 K_3 K_4) K_6) + \tau_2^\alpha \xi_2^\alpha (\kappa_1 K_4 K_6 + \kappa_1 K_4 K_5 + \kappa_1 K_4^2 + \kappa_1 K_3 K_4),$$

$$A_2 = [K_3 K_4 K_5 K_6 (1 - \mathcal{R}_c) + (K_5^2 + (K_4 + K_3) K_5) K_6^2 \\ + \xi_1^\alpha \tau_2^\alpha ((K_5^2 + (K_4 + K_3) K_5) K_6 + (K_4 + K_3) K_5^2 + K_3 K_4 K_5) + (K_4 + K_3) K_5^2 K_6] \kappa \\ + \tau_1^\alpha \kappa_1 K_3 K_4 K_5 K_6 (1 - \mathcal{R}_c) + \tau_1^\alpha (\kappa_1 K_4 K_5 + \kappa_1 K_4^2 + \kappa_1 K_3 K_4) K_6^2 + \tau_1^\alpha \kappa_1 K_4^2 K_5 K_6 + \tau_1^\alpha \kappa_1 K_3 K_4^2 K_6 \\ + \tau_2^\alpha \xi_2^\alpha ((\kappa_1 K_4 K_5 + \kappa_1 K_4^2 + \kappa_1 K_3 K_4) K_6 + (\kappa_1 K_4^2 + \kappa_1 K_3 K_4) K_5 + \kappa_1 K_3 K_4^2),$$

$$A_1 = [(K_5 + K_6 + \xi_1^\alpha \tau_2^\alpha) K_3 K_4 K_5 K_6 (1 - \mathcal{R}_c) + (K_4 + K_3) K_5^2 K_6^2 + \xi_1^\alpha \tau_2^\alpha K_5^2 ((K_4 + K_3) K_6 + K_3 K_4)] \kappa \\ + \xi_2^\alpha \tau_2^\alpha \kappa_1 K_4 [K_3 K_5 K_6 (1 - \mathcal{R}_c) + (K_4 K_5 K_6 + K_3 K_4 K_6 + K_3 K_4 K_5)] \\ + \tau_1^\alpha \kappa_1 K_4 K_6 [K_3 K_5 (K_6 + K_4) (1 - \mathcal{R}_c) + K_4 K_6 (K_5 + K_3)],$$

$$A_0 = K_3 K_4 K_5 K_6 (K_5 \kappa (K_6 + \xi_1^\alpha \tau_2^\alpha) + \kappa_1 K_4 (\tau_1^\alpha K_6 + \tau_2^\alpha \xi_2^\alpha)) (1 - \mathcal{R}_c).$$

It is clear that roots of Φ_1 have negative real parts. Note that coefficients A_4 and A_3 are always positive, while coefficients A_2 , A_1 and A_0 are positive whenever \mathcal{R}_c is less than one. It follows that roots of Φ_1 have negative real parts if the following Routh-Hurwitz conditions $\mathcal{H}_1 = A_3 A_2 - A_1 > 0$, $\mathcal{H}_2 = A_1 A_2 A_3 - A_3^2 A_0 - A_1^2 > 0$ hold. We thus claim what follows:

Lemma 6. *If $\mathcal{R}_c < 1$, then the disease-free equilibrium \mathcal{E}_0 of the fractional model (24) is locally asymptotically stable in Σ provided that the following conditions*

$$A_3A_2 - A_1 > 0 \quad \text{and} \quad A_1A_2A_3 - A_3^2A_0 - A_1^2 > 0 \quad (40)$$

hold, where A_4, A_3, A_2, A_1 and A_0 are coefficients of polynomial Φ_2 in (39).

For the global asymptotic stability of the disease-free equilibrium of the fractional model, we have the following result:

Theorem 8. *The disease-free equilibrium \mathcal{E}_0 of the fractional model (24) is globally asymptotically stable in Σ when $\mathcal{R}_c < 1$ provided that condition given by Eq. (16) holds.*

Proof. The proof of Theorem 8 follows the proof of Theorem 1. Let us consider the following Lyapunov function $\mathcal{K}(S, V, L, I_a, I_{ac}, I_c) = w'W^{-1}(L, I_a, I_{ac}, I_c)'$ where w' is the left eigenvector of the next generation matrix (NGM) $W^{-1}Z$ corresponding to the eigenvalue \mathcal{R}_c . Its derivative along the trajectories of (24) is given by

$$\mathbb{D}_t^\alpha \mathcal{K} = (\mathcal{R}_c - 1) w'(L, I_a, I_{ac}, I_c) - w'W^{-1}\mathcal{M}(S, V, L, I_a, I_{ac}, I_c) \leq 0.$$

Since the matrix $\mathcal{M}(S, V, L, I_a, I_{ac}, I_c) \geq \mathbf{0}_{\mathbb{R}^4}$ whenever condition given by Eq. (16) holds, it follows that $\mathbb{D}_t^\alpha \mathcal{K} < 0$ whenever $\mathcal{R}_c < 1$, with $\mathbb{D}_t^\alpha \mathcal{K} = 0$ if and only if $(L, I_a, I_{ac}, I_c) = \mathbf{0}_{\mathbb{R}^4}$. It follows that the largest invariant set contained in $\{(S, V, L, I_a, I_{ac}, I_c) \in \mathbb{R}_+^6 : \mathbb{D}_t^\alpha \mathcal{K} = 0\}$ is $\{\mathcal{E}_0\}$. Thus, from LaSalle Invariance Principle [38], every solution of (24) with initials conditions in Σ converge to \mathcal{E}_0 when $t \rightarrow +\infty$. That is $(L, I_a, I_{ac}, I_c) \rightarrow (0, 0, 0, 0)$, $S \rightarrow S_0$ and $V \rightarrow V_0$ when $t \rightarrow +\infty$, which is equivalent to $(S, V, L, I_a, I_{ac}, I_c) \rightarrow (S_0, V_0, 0, 0, 0, 0)$ when $t \rightarrow +\infty$. Thus, the disease-free equilibrium \mathcal{E}_0 is globally asymptotically stable in Σ whenever $\mathcal{R}_c < 1$. \square

5. Model calibration, forecasting and Numerical simulations

5.1. Model calibration and forecasting

We consider the yearly infected reported cases in Nigeria from 2010 to 2021 []. Due to the limitations of data compared to the number of model parameters, we assume some parameter values and fitted the others. Initial conditions are taken as follows: $S(0) = 156,077,013$, $V(0) = 4,830,000$, $L(0) = 37,150$, $I_a(0) = 18,575$, $I_{ac}(0) = 18,575$, $I_c(0) = 74$, $R(0) = 18,612$. The nonlinear least squares approach is utilized to accurately fit the HBV model to actual data, providing realistic parameter values for forecasting illness progression over a specified time frame. After numerically addressing the following optimization problem:

$$\min_{\Theta} \|\mathcal{I}_{predict} - \mathcal{I}_{data}\|_2, \quad (41)$$

where $\Theta = \{\beta, \sigma, \delta, \xi_1, \xi_2, \nu_1, \nu_2, \varrho\}$, We get the results shown in Table 1. The control reproduction number calculated using the parameter values in Table 1 is $\mathcal{R}_c \approx 1.766$. Figure 2 shows the comparison between model simulations and data fitting.

Table 1: Model parameters and their estimated values.

Parameter	Value	Source	Parameter	Value	Source
N_0	161×10^6	[46]	γ	1/52.68	[47]
Λ	$N_0 \times \gamma$	Estimated	p	0.85	[48]
ζ	0.5	Assumed	q	3%	Assumed
κ	0.5	Assumed	τ_1	0.5	Assumed
τ_2	0.5	Assumed	ω	1/30	[49]
σ	0.000400641026003	Fitted	β	0.342187729874554	Fitted
δ	0.081875992123649	Fitted	ξ_1	0.000000000533322	Fitted
ξ_2	0.845733030140545	Fitted	ν_1	0.428124741555356	Fitted
ϱ	0.000080020401110	Fitted	ν_2	0.477716811748168	Fitted

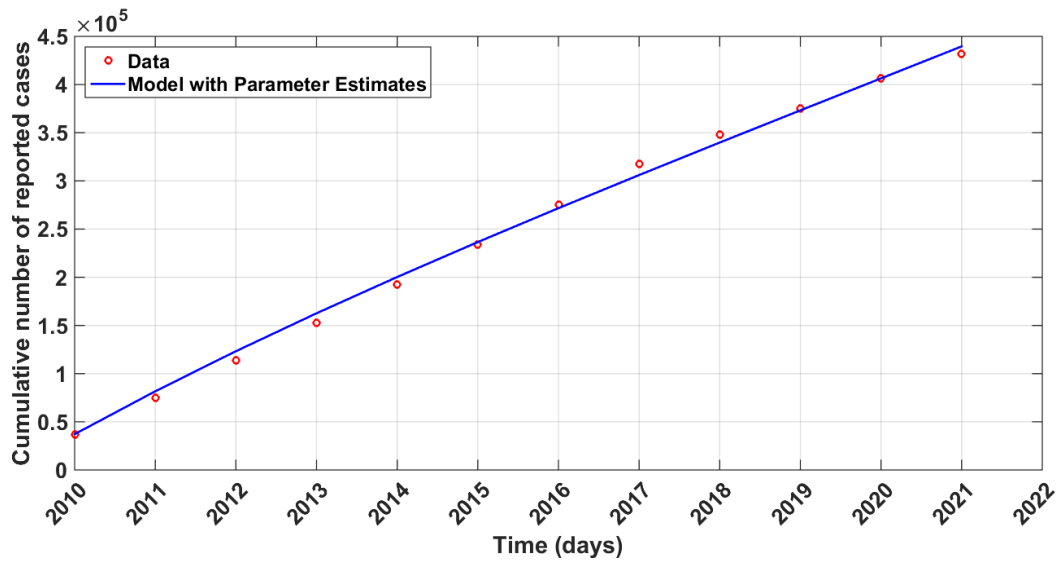


Figure 2: Model fitting versus HBV reported cases in Nigeria during the period from 2010 to 2021.

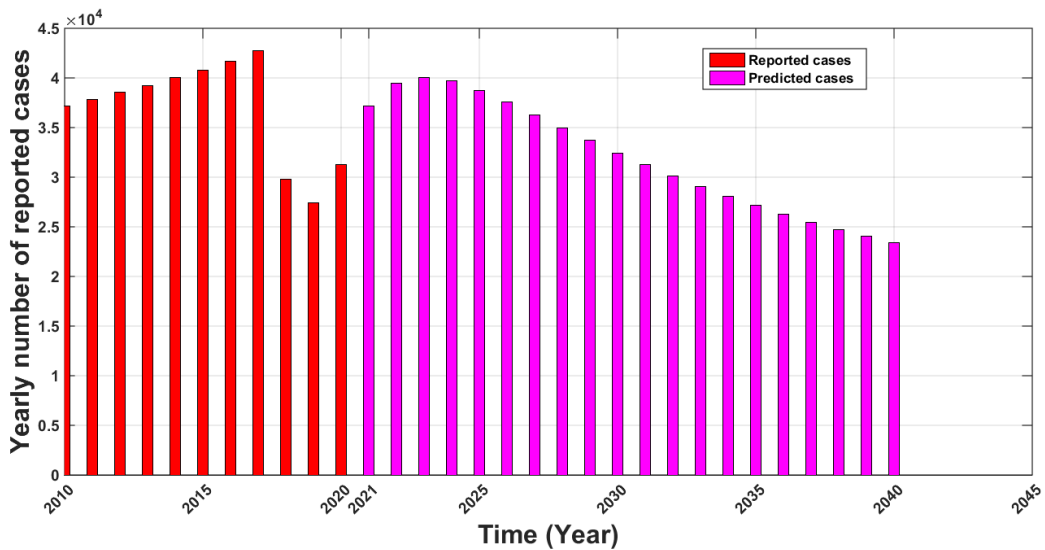


Figure 3: Model prediction of news cases

5.2. Numerical simulations

A variety of analytical and numerical methods have been developed to solve fractional differential equations (FDEs), the majority of which lack accurate analytic solutions. To construct a numerical scheme for the fractional model (5), we employed the Adams-Bashforth method based on the predictor-corrector iterative scheme [50, 51], as explained as follows.

Let us analyze the uniform discretization of $[0, \mathbf{a}]$ given by $t_i = i\aleph$, $i \in [0; \mathbf{N}] \cap \mathbb{N}$ where $\aleph = a/i$ denotes the step size. For a given approximation $\mathbf{x}_\aleph(t_j) \approx \mathbf{x}(t_j)$, the next approximation $x_\aleph(t_{j+1})$ is obtained (using the predictor-corrector method) as follows:

$$\text{Predictor: } \mathbf{x}_\aleph^p(t_{m+1}) = \sum_{k=0}^{-1+[\Psi]} \frac{t_{m+1}^k}{k!} x_0^k + \frac{1}{\Gamma(\varphi)} \sum_{k=0}^m d_{k,j+1} \mathbb{O}(t_k, x_\aleph(t_k));$$

$$\text{Corrector: } x_h(t_{m+1}) = \sum_{k=0}^{[\Sigma]-1} \frac{t_{m+1}^k}{k!} x_0^k + \frac{\aleph^\Psi}{\Gamma(2+\Psi)} \mathbb{O}(t_{k+1}, x_\aleph^\aleph(t_{k+1})) + \frac{\aleph^\Psi}{\Gamma(2+\Psi)} \sum_{k=0}^i b_{k,j+1} \mathbb{O}(t_k, x_\aleph(t_k));$$

with

$$b_{k,n+1} = \begin{cases} n^{1+\Psi} - (m-\Psi)(n+1)^\Psi, & \text{if } k=0, \\ (n-k+2)^{1+\Psi} + (n-k)^{1+\Psi} - 2(n-k+1)^{1+\Psi}, & \text{if } 1 \leq k \leq n, \\ 1 & \text{if } k=n+1, \end{cases}$$

$$\text{and } d_{k,n+1} = \frac{\aleph^\Psi}{\Psi} \left[(n-k+1)^\Psi - (n-k)^\Psi \right].$$

The stability, convergence and accuracy of the above scheme can be found in [52, 50]. Note that this algorithm was implemented by Garrappa in Matlab software through the package namely **fde12** [53].

Figure 4 depicts the comparison of the Runge-kutta of order 4, and the Adams-Bashforth method. We see that for the fractional order parameter value $\alpha = 1$, the both methods coincide, that is $\mathbb{D}^\alpha \equiv \frac{d}{dt}$.

Figure 5 depicts model solution of infected states variables of the HBV model where the fractional order parameter $\alpha = 1$, and with different initial conditions. Parameter values are listed in table 1, which give $\mathcal{R}_c \approx 1.766$. In this case, all trajectories tend to the endemic equilibrium state.

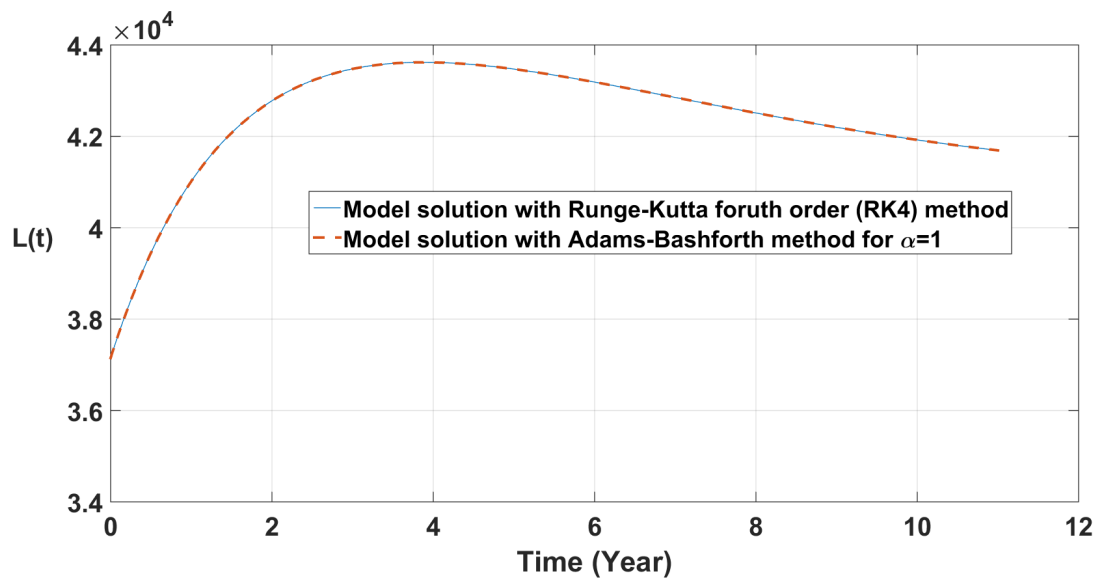
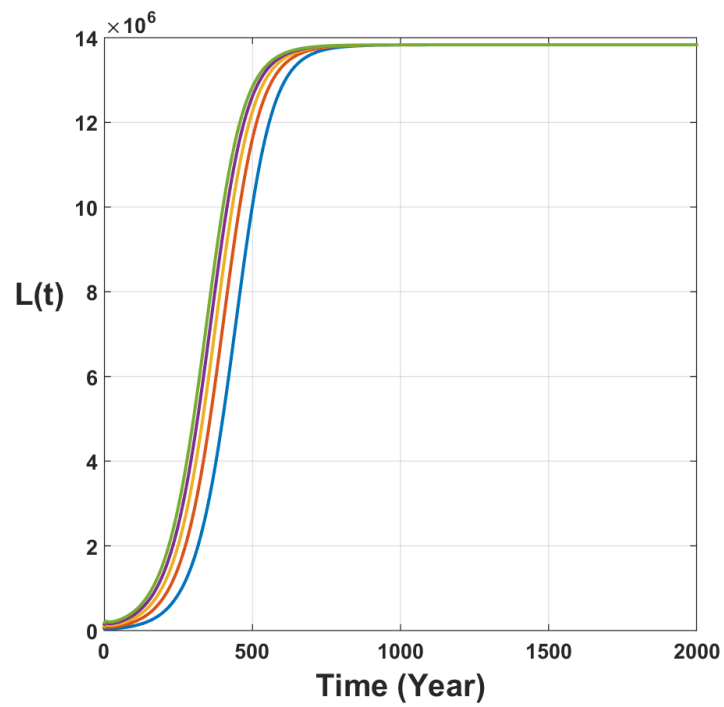
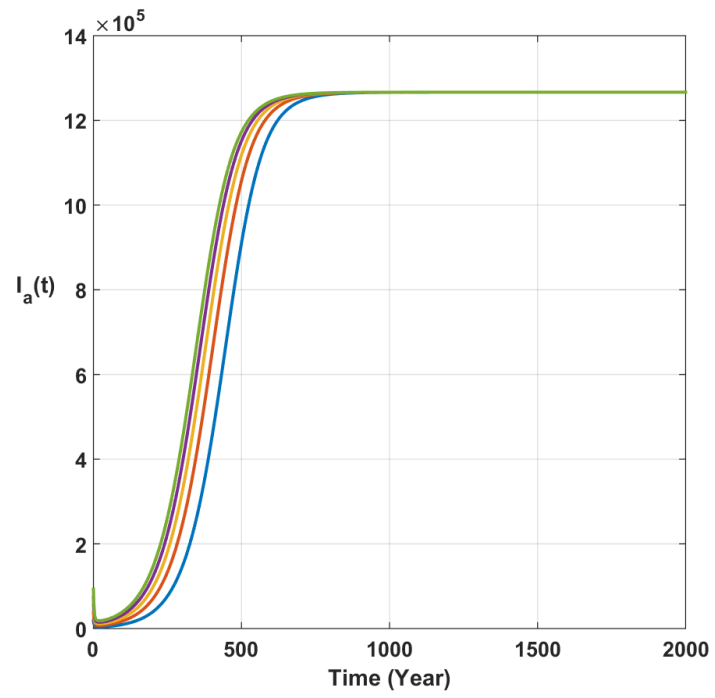


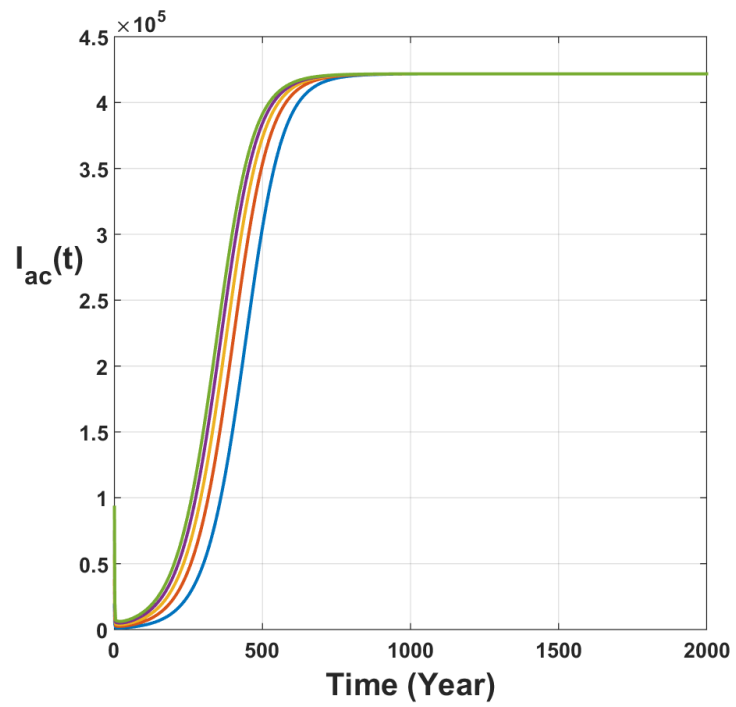
Figure 4: Model solution with two numerical methods: Runge-kutta fourth order (RK4) and Adams-Bashford method, for $\alpha = 1$.



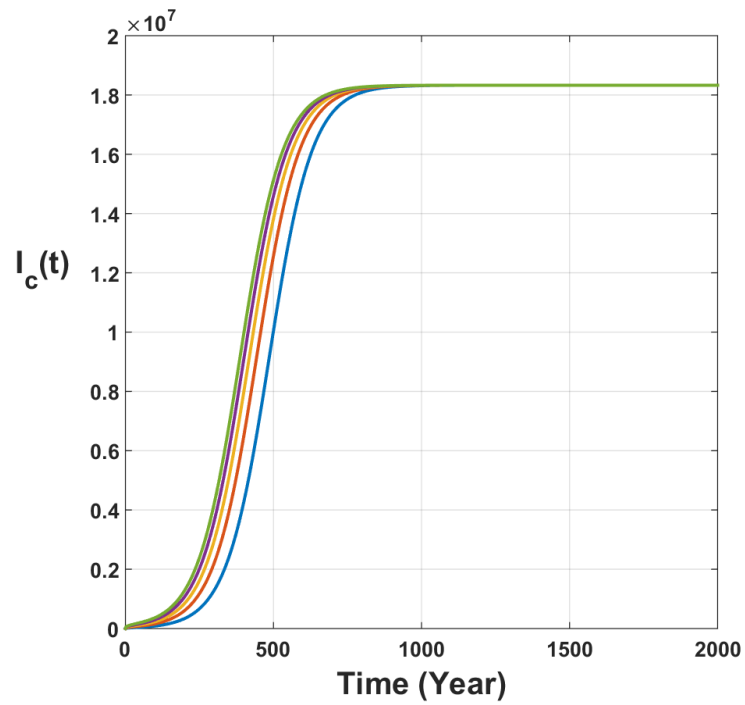
(a) Individuals in Latent stage



(b) Acute infected individuals

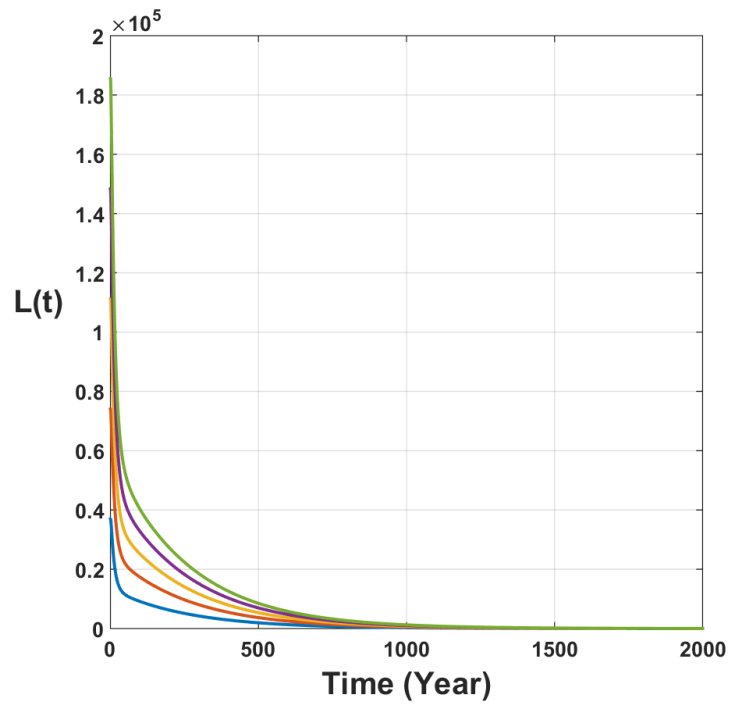


(c) Asymptomatic carrier individuals

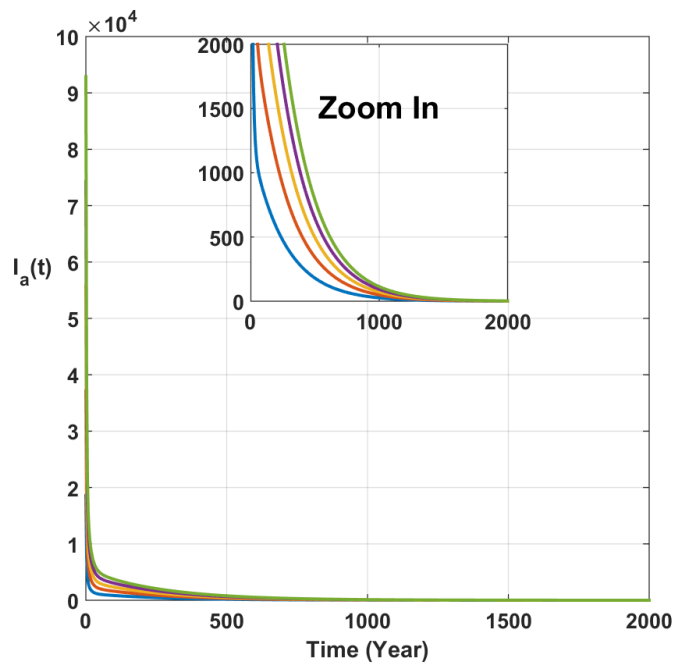


(d) Carrier individuals

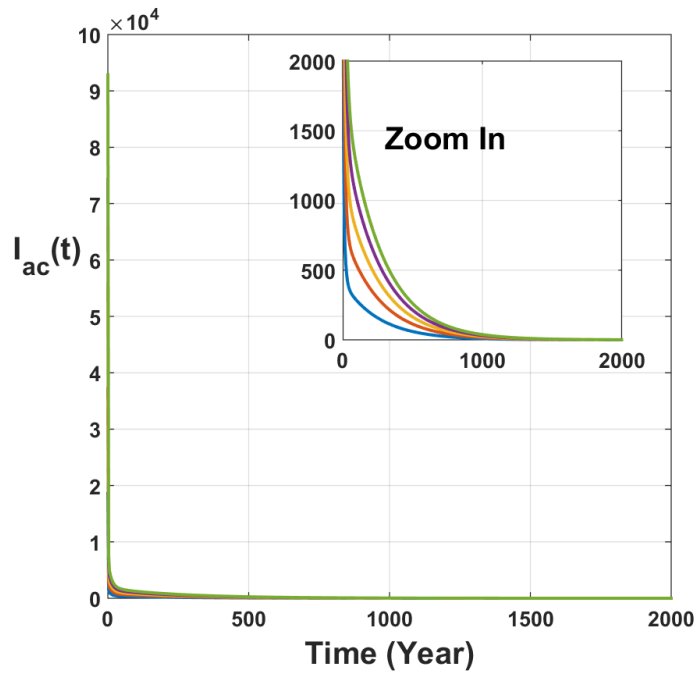
Figure 5: Times-series of infected states of fractional model with different initial conditions and the fractional order parameter $\alpha = 1$. Parameter values are listed in table 1, which give $\mathcal{R}_c \approx 1.766$.



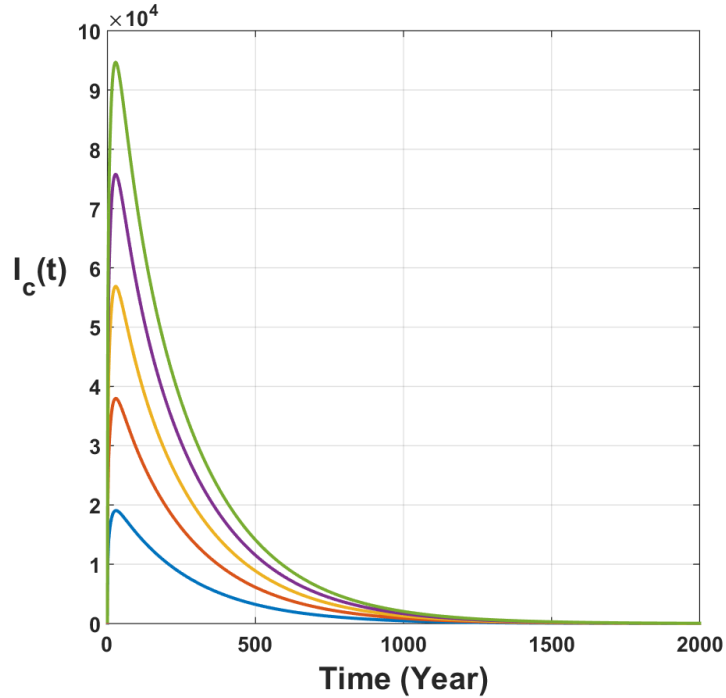
(a) Individuals in Latent stage



(b) Acute infected individuals



(c) asymptomatic carrier individuals

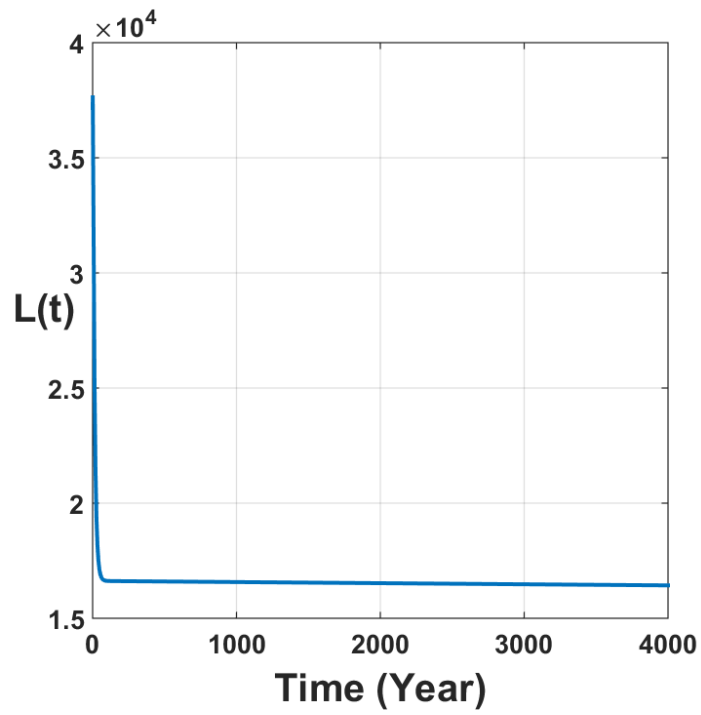


(d) Carrier individuals

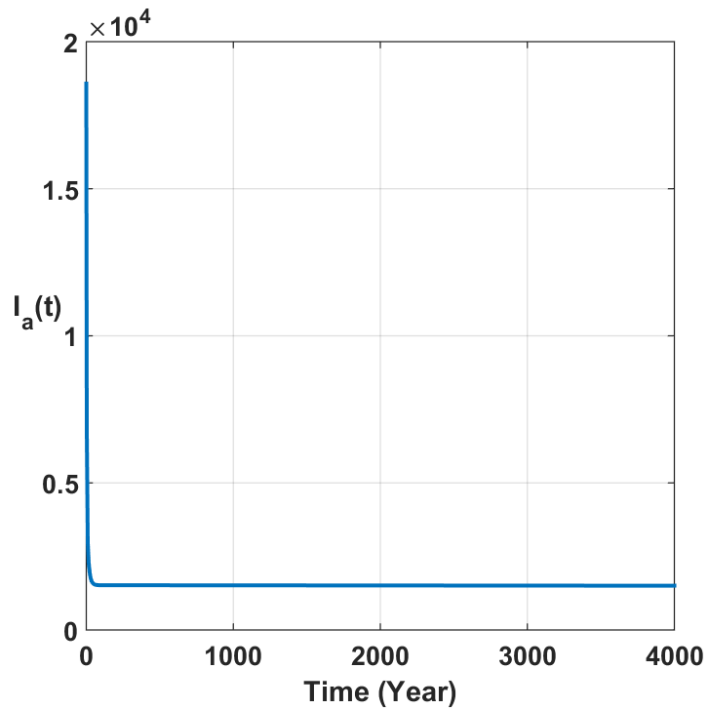
Figure 6: Times-series of infected states of fractional model with different initial conditions and the fractional order parameter $\alpha = 1$. Parameter values are listed in table 1, except which $\beta = 0.15$ such that $\mathcal{R}_c = 0.7741 < 1$.

Figure 6 illustrates the GAS of the disease-free equilibrium. We see that all trajectories tend to the disease-free for $\mathcal{R}_c = 0.7741 < 1$. Nevertheless, when we set $\beta = 0.19$ such that the value of the control reproduction number \mathcal{R}_c is near, but less than, one ($\mathcal{R}_c = 0.9805 < 1$), the trajectories of infected states variables tend to the endemic equilibrium, which suggests that the backward bifurcation phenomenon can be occurred in the model. Note that, this phenomenon occurs in an epidemiological model when the locally stable disease-free equilibrium coexists with a locally stable endemic equilibrium whenever the epidemiological threshold called the basic reproduction number is less than one ($\mathcal{R}_0 < 1$). In this case, it is not sufficient to decrease the value of \mathcal{R}_0 under one to the disease extinction. Some extra efforts must be made to reach the disappearance of the disease.

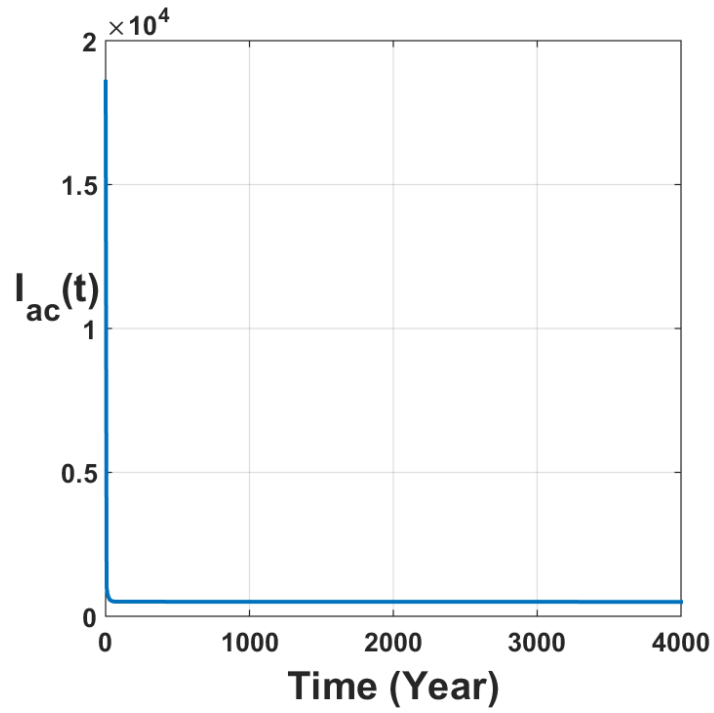
In figure 8, we see that when the fractional order parameter α vary, the density of individuals in latent stage as well as those in carrier stage decrease.



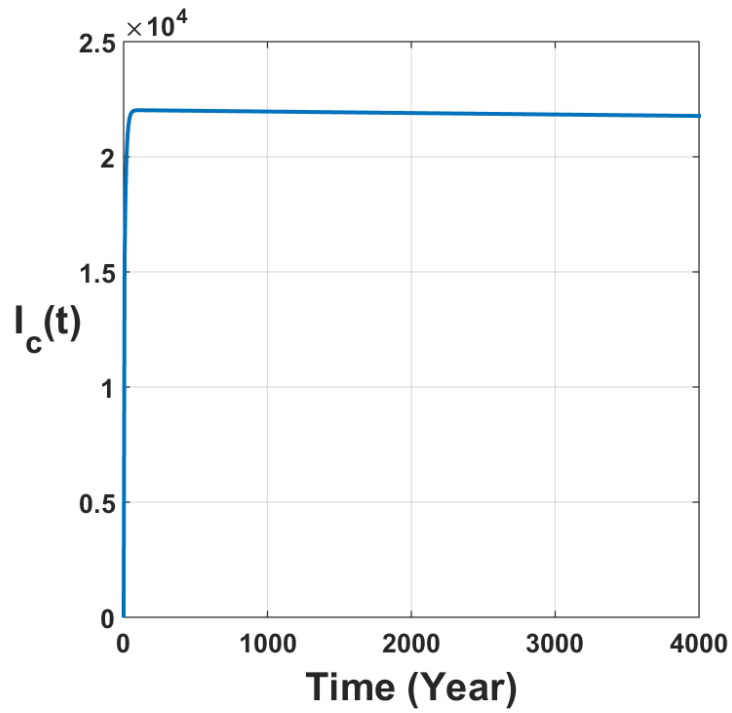
(a) Individuals in Latent stage



(b) Acute infected individuals

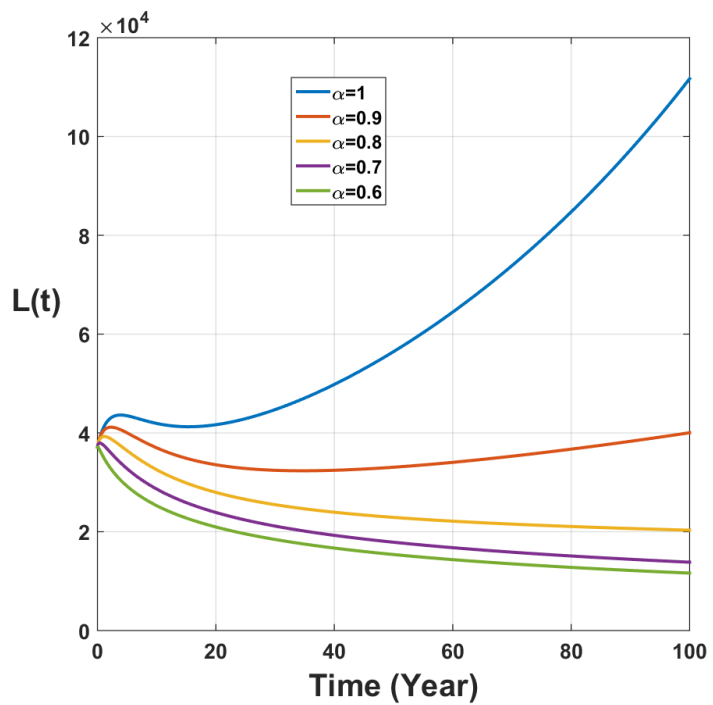


(c) asymptomatic carrier individuals

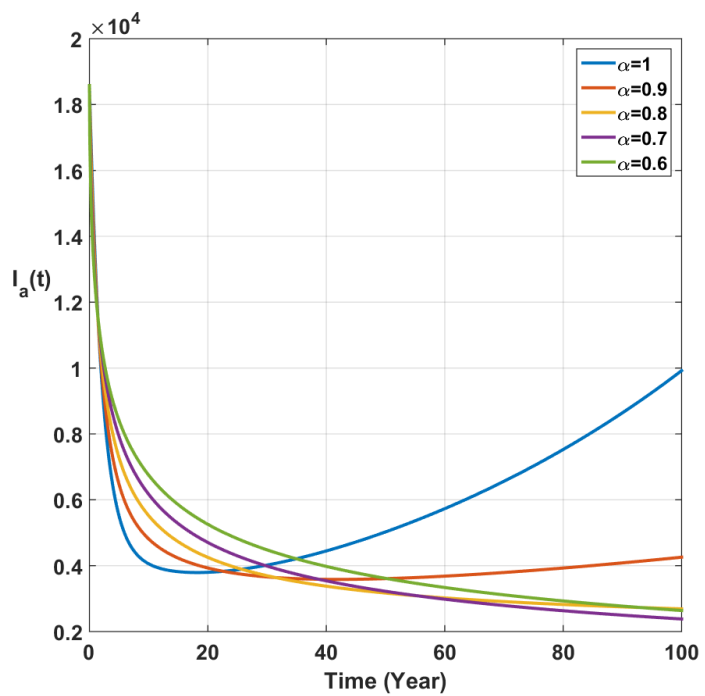


(d) Carrier individuals

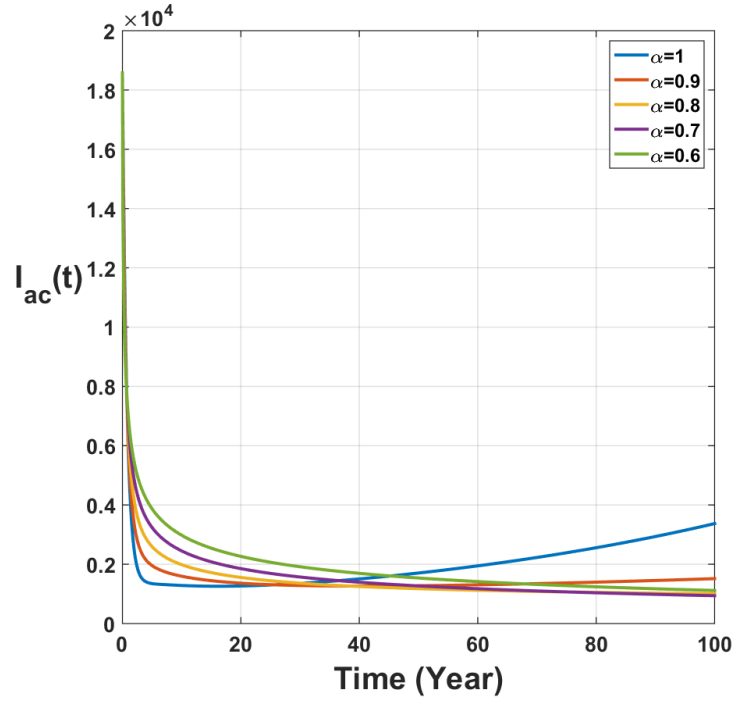
Figure 7: Times-series of infected states of fractional model with different initial conditions and the fractional order parameter $\alpha = 1$. Parameter values are listed in table 1, except which $\beta = 0.19$ such that $\mathcal{R}_c = 0.9805 < 1$.



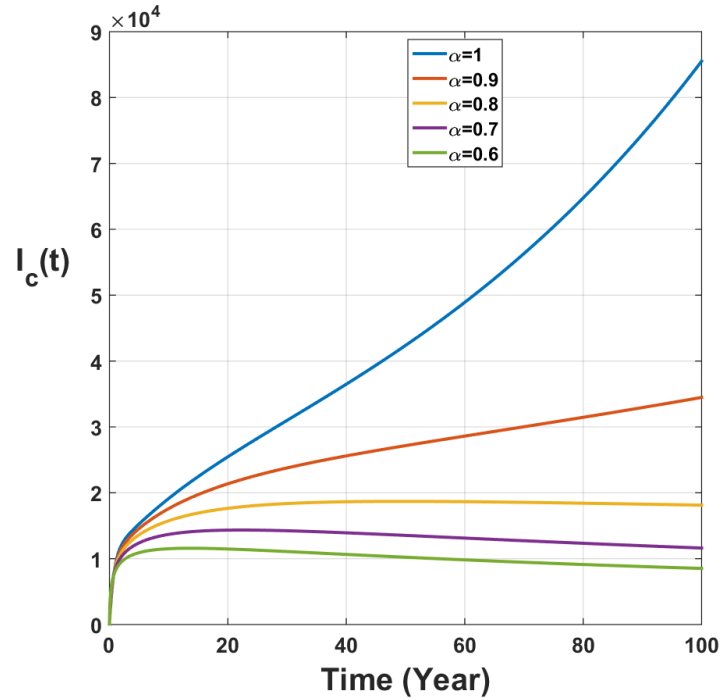
(a) Individuals in Latent stage



(b) Acute infected individuals



(c) Asymptomatic carrier individuals



(d) Carrier individuals

Figure 8: Times-series of infected states of fractional model with different values of the fractional order parameter α . Parameter values are listed in table 1, which give $\mathcal{R}_c \approx 1.766$.

Figure 9 illustrates \mathcal{R}_c as a function of fractional order α , an increasing function within the range of $[0.3; 1]$, while a decreasing function in the range $(0, 0.3)$, with Rc equal to 1

around $\alpha \approx 0.16$ and $\alpha \approx 0.72$.

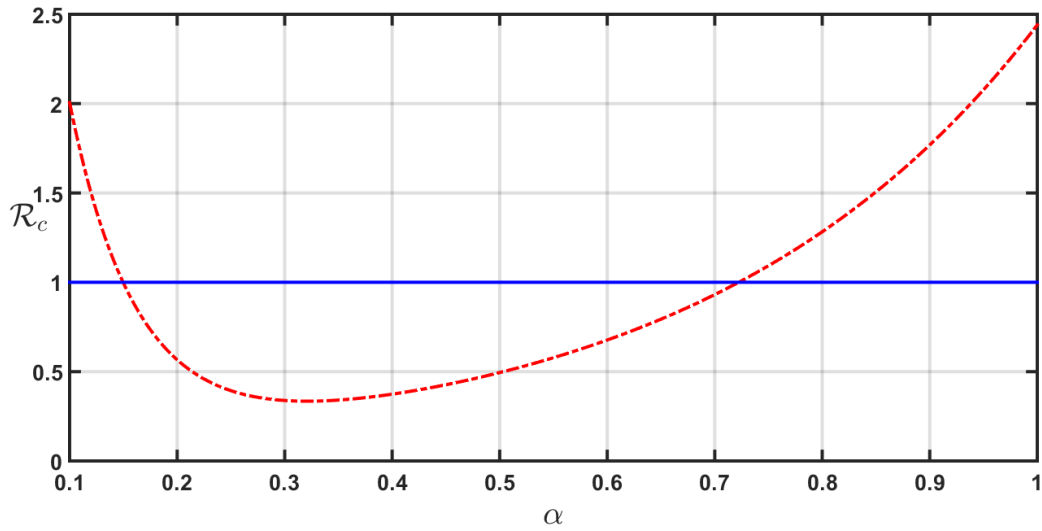
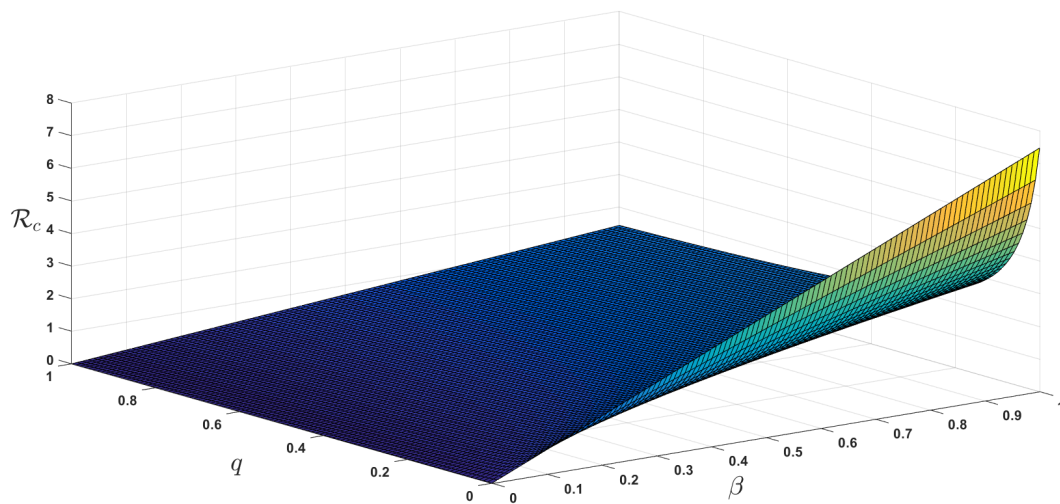
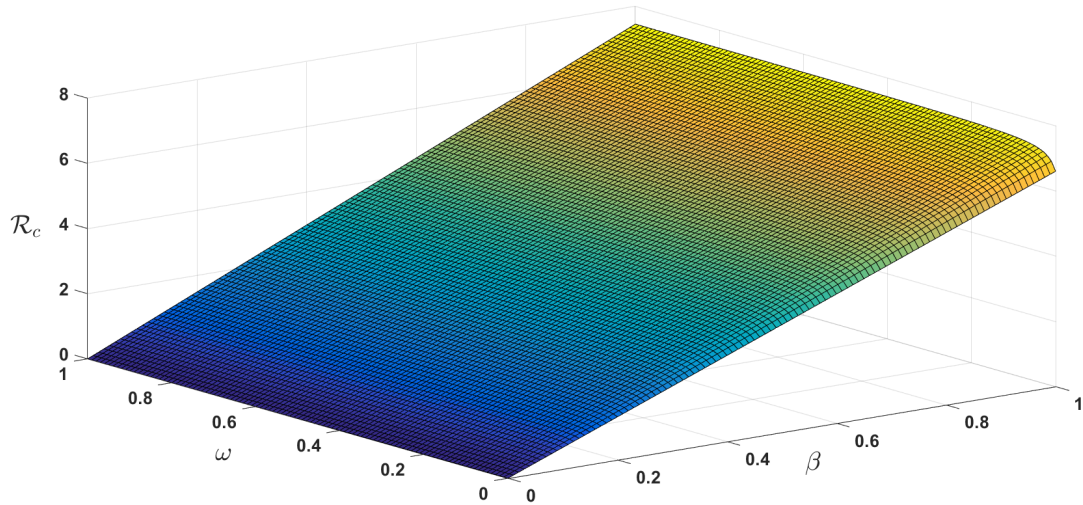


Figure 9: 3-D plot of \mathcal{R}_c as a function of the fractional order parameter α .

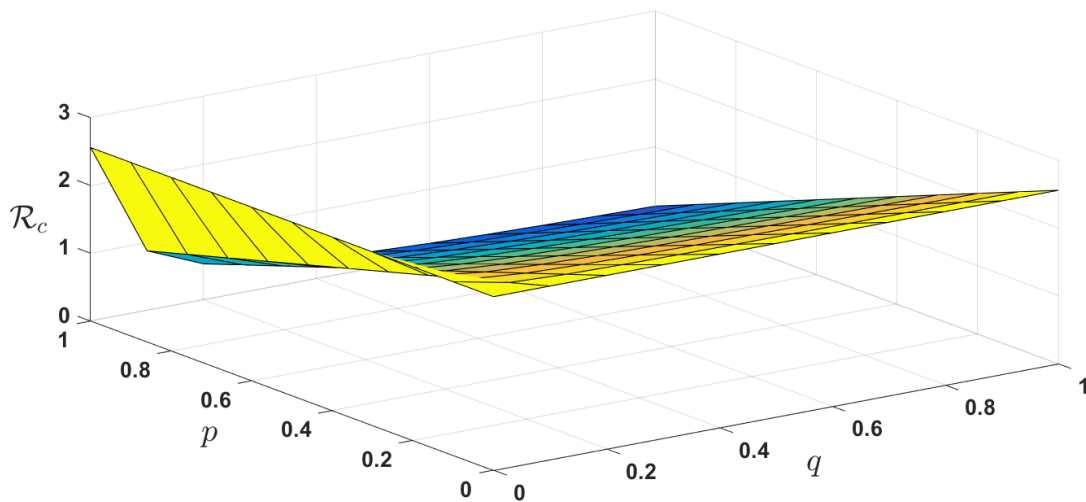
Figure 10 illustrates \mathcal{R}_c as a function of some model parameters while the other model parameters are fixed and listed in table 1 . In panel (a), the control reproduction number increases with the parameter β and decreases when q increases. From panel (b), it follows that \mathcal{R}_c is a increasing function of β and ω , while its value decreases when q increases.



(a) 3-D plot of \mathcal{R}_c as a function β and q



(b) 3-D plot of \mathcal{R}_c as a function β and ω



(c) 3-D plot of \mathcal{R}_c as a function q and p

Figure 10: 3-D plot of \mathcal{R}_c as a function of the some model parameters. The values of others parameters are fixed and listen in table 1.

6. Conclusion

This work dealt with the mathematical modeling of Hepatitis B Virus (HBV) transmission dynamics in which we considered imperfect vaccine, with both integer and Caputo fractional order derivatives. After the model formulation, we computed the control reproduction number \mathcal{R}_c , and prove the local and global asymptotic stability of the hepatitis B-free equilibrium point under conditions whenever $\mathcal{R}_c < 1$. We prove also the existence of endemic equilibrium points and found that there is a possibility of occurrence of backward bifurcation phenomenon whenever $\mathcal{R}_c < 1$ is near, but less than one. The existence and uniqueness of solution of the fractional model as well as its global stability are performed

using respectively the Banach contraction principle and the Ulam-Hyers method. Using reported cases in Nigeria, a Sub-Saharan country in which Hepatitis B is endemic, we calibrate the model by performing parameter estimation. This permits to found that $\mathcal{R}_c \approx 1.766$. The forecast for several years permits to confirm that Hepatitis B will remain a health problem in this country. We then construct a numerical scheme for our fractional model and perform numerical simulations to validate the obtained theoretical results, as well as to see the impact of varying the fractional order parameter α .

In the future direction, we plan to perform sensitivity analysis to determine key parameters which play a important role on the hepatitis B virus transmission dynamics, and thus formulate the problem as a optimal control problem, to determinate which strategy is better than which ones already are applying in Nigeria.

Competing Interests

The authors declare no conflicts of interest.

Data availability

The sources of data used in this work are mentioned in the text.

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