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Hepatitis b infection and its control: Deterministic & stochastic analysis

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Abstract

This article concentrates on the analysis of HBV infection with susceptible, asymptomatic, chronic, hepatocellular carcinoma developed, compensated cirrhosis developed, decompensated cirrhosis developed and recovered individuals. Global stability of disease free equilibrium in terms of reproduction number (R_0) is analyzed. Persistence of the disease is studied. Through numerical simulations we validate the results. The effect of environmental fluctuations is also addressed in the model system by numerical simulations which suggest that the system is robust under stochastic perturbation.

Keywords: Hepatitis B, stability, persistence, white noise

1. Introduction

Hepatitis B, a potentially life-threatening liver infection, puts people at high risk of death from cirrhosis of the liver and liver cancer. It is found that more than 240 million people have long-term chronic liver infections and more than 780000 people die each year due to acute or chronic consequences of hepatitis B [1]. This infection is either acute or chronic and can vary from asymptomatic infection or mild disease to severe or rarely fulminant hepatitis. Acute hepatitis B is usually self-limiting in nature with a case fatality rate of 0.5–1% [2]. This infection is chronic if HBsAg persists more than six months and it leads to develop chronic liver disease infection and hepatocellular carcinoma (HCC) in due course of time [3]. In hyper-endemic areas transmission of HBV occurs by perinatal, percutaneous, sexual exposure and close person-to-person contact [4]. 5–10% of the adult population is chronically infected with Hepatitis B prevalence in sub-Saharan Africa and East Asia. In Middle East and Indian subcontinent about 2–5% of the population is chronically infected along with nearly 1% of the population in Western Europe and North America [5].

Considering a compartmental model of HBV transmission with susceptible, exposed, acute, carrier, immuned and migrated class Khan *et al.* [6] found that number of infected individuals and number of migrated individuals is related by direct proportion. Kamyad *et al.* [7] proposed a mathematical model consisting of susceptible, exposed, acute, chronic HBV carriers and recovered individuals with two controls strategies vaccination and treatment for hepatitis B virus. They investigated existence of equilibria and their stability based on numerical simulation and pointed out different control measures and remarked that there is still a lot to do in this area. Long *et al.* [8] studied a mathematical model consists of uninfected hepatocytes, infected hepatocytes, total host hepatocytes, free virus and a CTL response and conclude that if the virus replicates slowly, the CTL response to HBV is able to eliminate the entire virus from the liver otherwise serious problem persists. Kimbir *et al.* [9] proposed a mathematical HBV model and suggested that the reproduction number reduces with vaccination and treatment. Zou *et al.* [10] proposed a HBV model with protective immunity and immune following vaccination and suggested an optimal control strategy with a combination of immunization of newborns, retroactive immunization of susceptible adults, and reduction of contacts. Zhang J and Zhang S studied hepatitis B virus with control strategies of newborn vaccination and treatment and highlighted some preventive measures using optimal control techniques [11].

Despite an effective vaccination program of newborn babies the incidence of hepatitis B is still increasing in India. As there is no specific treatment for acute hepatitis B care should be taken on comfort and adequate nutritional balance, including replacement of fluids. People with chronic Hepatitis B may administer drugs including oral antiviral agents with interferon injections and this can slow down incidence of HCC and improve long term survival. But the success rate of vaccine is still insignificant. Surgery, chemotherapy and liver transplants can prolong life for up-to a few years. It is interesting to note that in most cases, infected adults can recover, but 5%–10% become chronically infected. About 30%–50% of patients with acute necrotizing vasculitis (polyarteritis nodosa) are HBV carriers [12]. Without immediate treatment nine out of 10 newborn babies who get HBV at birth will develop chronic infection and become HBV carriers.

Hepatitis B infection whose model flow diagram is given in Figure 1. Further the dynamics of HBV infection is highly complex and its progression is non-linear and not sequential with several recognizable phases of variable duration. Hence it is highly essential to study the dynamical behavior of HBV infection properly. However, for more accurate study of HBV characteristics and better insight of practical application, more factors that influence the transmission of HBV should be incorporated in the model with some high risk group or at smaller spatial scales. Again so far we know, none of the studies include Hepatocellular carcinoma developed, compensated cirrhosis developed and decompensated cirrhosis developed individuals into the model system. We think that these classes have some important roles into the HBV model system and as a result the main thrust of the paper is to study the dynamical behavior of this Hepatitis B infection with the inclusion of such classes together with some prevention strategies.

2. Model

We formulate a mathematical model to study the dynamics of

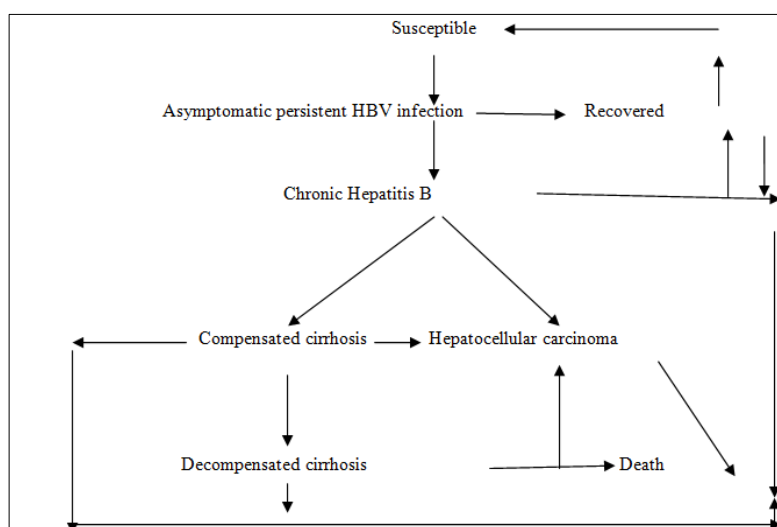


Fig 1: Further the dynamics of HBV infection is highly complex and its progression is non-linear and not sequential with several recognizable phases of variable duration

Our proposed model is as follows:

$$\begin{aligned}
 \frac{dS(t)}{dt} &= b - (\gamma A + \delta C) \frac{S}{N} - \mu S + (1 - \tau)\psi R \\
 \frac{dA(t)}{dt} &= (\gamma A + \delta C) \frac{S}{N} - (\mu + \alpha + k)A + \tau\psi R \\
 \frac{dC(t)}{dt} &= kA - (\mu + \varepsilon + \beta + \xi)C \\
 \frac{dH(t)}{dt} &= \phi\varepsilon C + \eta\rho X - (\mu + \xi)H + \sigma Y \\
 \frac{dX(t)}{dt} &= (1 - \phi)\varepsilon C - (\rho + \mu + \xi)X \\
 \frac{dY(t)}{dt} &= (1 - \eta)\rho X - (\mu + \xi + \sigma)Y \\
 \frac{dR(t)}{dt} &= \alpha A + \beta C - (\mu + \psi)R
 \end{aligned}
 \tag{1}$$

Where

$$N(t) = S(t) + A(t) + C(t) + H(t) + X(t) + Y(t) + R(t)$$

Here S is the number of susceptible, A is the number of asymptomatic, C is the number of chronic, H is the Hepatocellular carcinoma developed, X is the number of compensated cirrhosis developed, Y is the number of decompensated cirrhosis developed and R is the number of recovered individuals at any time t . Further b is the birth or recruitment rate, μ is the mortality rate, ξ is the disease induced death rate, γ is the effective contact rate with asymptomatic individuals, δ is the effective contact rate with chronic individuals, α is the recovery rate due to antiviral therapy or vaccination for asymptomatic class, β is the recovery rate due to antiviral therapy or vaccination for chronic class, k is the rate of propagation to chronic class, ψ is the rate at which a part of recovered individuals become infected and remaining become susceptible, ρ is the rate at which a part of compensated cirrhosis developed individuals become Hepatocellular carcinoma developed individuals and remaining become decompensated cirrhosis developed individuals. ε is the rate at which a part of chronic individuals become Hepatocellular carcinoma developed individuals and remaining become compensated cirrhosis developed individuals. σ is the rate of propagation to Hepatocellular carcinoma developed individuals from decompensated cirrhosis developed individuals. Further τ, ϕ, η are the parameters lying between 0 and 1.

3. Disease Free Equilibrium and Reproduction Number

The Disease Free Equilibrium (DFE) of the model is given by $E_0(\frac{b}{\mu}, 0, 0, 0, 0, 0)$. Further the associated next generation

$$F = \begin{pmatrix} \gamma & \delta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

matrices are given by and

$$V = \begin{pmatrix} k + \alpha + \mu & 0 & 0 & 0 & 0 & -\tau\psi \\ -k & \beta + \varepsilon + \xi + \mu & 0 & 0 & 0 & 0 \\ 0 & -\varepsilon\phi & \xi + \mu & -\eta\rho & -\sigma & 0 \\ 0 & -\varepsilon(1-\phi) & 0 & \xi + \mu + \rho & 0 & 0 \\ 0 & 0 & 0 & -(1-\eta)\rho & \xi + \mu + \sigma & 0 \\ -\alpha & -\beta & 0 & 0 & 0 & \mu + \psi \end{pmatrix}$$

Hence Reproduction number,

$$R_0 = \rho(FV^{-1}) = \frac{(\beta\gamma + k\delta + \gamma(\varepsilon + \xi + \mu))(\mu + \psi)}{(\beta + \varepsilon + \xi + \mu)(\mu(\mu + \psi) + \alpha(\mu + \psi - \tau\psi)) + k((\varepsilon + \xi + \mu)(\mu + \psi) + \beta(\mu + \psi - \tau\psi))} \tag{2}$$

Now, using Theorem 2 (van den Driessche P. *et al.*) we have established the following result.

Theorem 1: The DFE of the model is LAS if $R_0 < 1$, and unstable if $R_0 > 1$.

The basic reproduction number (R_0) measures the average number of new infections generated by a single infected individual in a completely susceptible population. Thus, Theorem 1 implies that the disease can be eliminated from the community (when $R_0 < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the DFE, E_0 . To ensure that elimination of the disease is independent of the initial sizes of the sub-populations, it is necessary to show that the DFE is globally-asymptotically stable. This is established below.

Theorem 2: (Castillo-Chavez *et al.* [13]) If the model can be written in the form

$$\frac{dX}{dt} = F(x, Z), \frac{dZ}{dt} = G(X, Z), G(x, 0) = 0 \tag{3}$$

where $X \in R^m$ denotes (its components) the number of uninfected individuals and $Z \in R^n$ denotes (its components) the number of infected individuals including latent, infectious, etc. $U_0 = (x^*, 0)$ denotes the disease-free equilibrium of the system.

And assume that (i) For $\frac{dX}{dt} = F(X, 0), X^*$ is globally asymptotically stable (GAS),

(ii) $G(X, Z) = AZ - \hat{G}(X, Z), \hat{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$, where $A = D_z G(X^*, 0)$ is an

M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model

makes biological sense. Then the fixed point $U_0 = (x^*, 0)$ is a globally asymptotic stable (GAS) equilibrium of model system (1) provided that $R_0 < 1$.

Applying Theorem 2 to the model gives $\hat{G}(X, Z) = \begin{pmatrix} \alpha\gamma + c\delta \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$

Since $\hat{G}(X, Z) \geq 0$ hence by Theorem 2, E_0 is GAS. Hence we summarize the result in Lemma 1.

Lemma 1: The DFE of the model, given by E_0 , is globally-asymptotically stable (GAS) whenever $R_0 \leq 1$.

4. Bondedness

Lemma2. The model system (1) is bounded.

Proof: Define, $m = \mu + \xi$. From model system (1) and using differential inequality argument we get $\frac{dN}{dt} = b - \mu S - \mu A - mC - mH - mX - mY - \mu R \Rightarrow \frac{dN}{dt} + \mu N \leq b \Rightarrow \lim_{t \rightarrow \infty} Sup N(t) \leq \frac{b}{\mu}$.

Hence the system defined in (1) is bounded.

5. Persistence

Theorem 3: The total Host population $N(t)$ is uniformly persistent whenever $N(0) > 0$.

Proof: Define, $m = \mu + \xi$. From model system (1) we get,

$$\frac{dN}{dt} = b - \mu S - \mu A - mC - mH - mX - mY - \mu R \Rightarrow \frac{dN}{dt} + mN \geq b.$$

Using differential inequality argument we have $\liminf_{t \rightarrow \infty} N(t) \geq \frac{b}{m}$. Hence the result.

Theorem 4: Suppose $A(t)$ is uniformly persistent then $C(t)$ is uniformly persistent whenever $C(0) > 0$.

Proof: Define, $A_\infty = \liminf_{t \rightarrow \infty} A(t)$. From 3rd equation of system (1) we have

$$\frac{dC}{dt} = kA - (\mu + \varepsilon + \beta + \xi)C \geq kA_\infty - (\mu + \varepsilon + \beta + \xi)C$$

If $C < \frac{kA_\infty}{\mu + \varepsilon + \beta + \xi}$ then $\frac{dC}{dt} \geq 0$ and hence $C(t)$ is unbounded. So, $C \geq \frac{kA_\infty}{\mu + \varepsilon + \beta + \xi}$.

Thus when $A(t)$ is uniformly persistent then $C(t)$ is uniformly persistent.

6. Stochastic Stability

Ecological systems are characteristically depends on fluctuate climate and natural disturbances. The recurrence of random drivers in bio-geophysical processes motivates the study of how a stochastic environment may affect and determine the dynamics of natural systems. We now extend the deterministic model (1) to analyze the role of random environmental fluctuations on stability. The random fluctuations make the parameters of the model to oscillate about their average values. We consider such randomness to the model (1) by incorporating additive white noises. The white noise perturbation included will change any parameter V of the model as $V + \alpha\chi(t)$, where α is the amplitude of the noise and $\chi(t)$ is a Gaussian white noise process at time t , but the deterministic and stochastic models have same equilibriums which will also now fluctuate about their mean states. By considering the randomly fluctuating driving forces in the form of additive noise to the model (1), we get the following stochastic model (2.1)-(2.7):

$$\frac{dS(t)}{dt} = b - (\gamma A + \delta C) \frac{S}{N} - \mu S + (1 - \tau)\psi R + \alpha_1 \chi_1(t) \tag{2.1}$$

$$\frac{dA(t)}{dt} = (\gamma A + \delta C) \frac{S}{N} - (\mu + \alpha + k)A + \tau\psi R + \alpha_2 \chi_2(t) \tag{2.2}$$

$$\frac{dC(t)}{dt} = kA - (\mu + \varepsilon + \beta + \xi)C + \alpha_3 \chi_3(t) \tag{2.3}$$

$$\frac{dH(t)}{dt} = \phi\varepsilon C + \eta\rho X - (\mu + \xi)H + \sigma Y + \alpha_4 \chi_4(t) \tag{2.4}$$

$$\frac{dX(t)}{dt} = (1 - \phi)\varepsilon C - (\rho + \mu + \xi)X + \alpha_5 \chi_5(t) \tag{2.5}$$

$$\frac{dY(t)}{dt} = (1 - \eta)\rho X - (\mu + \xi + \sigma)Y + \alpha_6 \chi_6(t) \tag{2.6}$$

$$\frac{dR(t)}{dt} = \alpha A + \beta C - (\mu + \psi)R + \alpha_7 \chi_7(t) \tag{2.7}$$

Here $\chi(t) = [\chi_1(t), \chi_2(t), \chi_3(t), \chi_4(t), \chi_5(t), \chi_6(t), \chi_7(t)]$ is a seven dimensional Gaussian white noise process agreeable $E[\chi_i(t)] = 0; i = 1, 2, 3, 4, 5, 6, 7; E[\chi_i(t)\chi_j(t')] = \delta_{ij}\delta(t-t'); i, j = 1, 2, 3, 4, 5, 6, 7$, where δ_{ij} is the Kronecker symbol; δ is the delta-Dirac function.

In this analysis, we emphasis on the dynamics of the model (2.1)-(2.7), about the interior equilibrium point $E^* (S^*, A^*, C^*, H^*, X^*, Y^*, R^*)$ in the line to the method introduced by Nisbet and Gurney [14] and Carletti [15].

Let $S(t) = u_1(t) + S_1^*; A(t) = u_2(t) + S_2^*; C(t) = u_3(t) + S_3^*; H(t) = u_4(t) + S_4^*; X(t) = u_5(t) + S_5^*; Y(t) = u_6(t) + S_6^*; R(t) = u_7(t) + S_7^*$ and by considering only the consequence of linear stochastic perturbations. Hence the

model (2.1)-(2.7) reduces to the following linear system
$$u_1'(t) = -\frac{1}{N}\gamma u_2 S_1^* - \frac{1}{N}\delta u_3 S_1^* + \alpha_1 \chi_1(t) \tag{2.3}$$

$$u_2'(t) = \frac{1}{N\gamma} u_1 S_2^* + \alpha_2 \chi_2(t) \tag{2.4}$$

$$u_3'(t) = 0 + \alpha_2 \chi_2(t) \tag{2.5}$$

$$u_4'(t) = 0 + \alpha_4 \chi_4(t) \tag{2.6}$$

$$u_5'(t) = 0 + \alpha_5 \chi_5(t) \tag{2.7}$$

$$u_6'(t) = 0 + \alpha_6 \chi_6(t) \tag{2.8}$$

$$u_7'(t) = 0 + \alpha_7 \chi_7(t) \tag{2.9}$$

Taking the Fourier transform of (2.3) - (2.9) we get,

$$\alpha_1 \mathcal{X}_1(\omega) = (i\omega) \mathcal{U}_1(\omega) + \left(\frac{1}{N}\gamma S_1^*\right) \mathcal{U}_2(\omega) + \left(\frac{1}{N}\delta S_1^*\right) \mathcal{U}_3(\omega) \tag{2.10}$$

$$\alpha_2 \mathcal{X}_2(\omega) = \left(-\frac{1}{N}\gamma S_2^*\right) \mathcal{U}_1(\omega) + (i\omega) \mathcal{U}_2(\omega) \tag{2.11}$$

$$\alpha_3 \mathcal{X}_3(\omega) = (i\omega) \mathcal{U}_3(\omega) \tag{2.12}$$

$$\alpha_4 \mathcal{X}_4(\omega) = (i\omega) \mathcal{U}_4(\omega) \tag{2.13}$$

$$\alpha_5 \mathcal{X}_5(\omega) = (i\omega) \mathcal{U}_5(\omega) \tag{2.14}$$

$$\alpha_6 \mathcal{X}_6(\omega) = (i\omega) \mathcal{U}_6(\omega) \tag{2.15}$$

$$\alpha_7 \mathcal{X}_7(\omega) = (i\omega) \mathcal{U}_7(\omega) \tag{2.16}$$

The matrix form of (2.10) and (2.16) is
$$M(\omega) \mathcal{U}(\omega) = \mathcal{X}(\omega) \tag{2.17}$$

$$M(\omega) = \begin{pmatrix} A_1 & A_2 & A_3 & A_4 & A_5 & A_6 & A_7 \\ B_1 & B_2 & B_3 & B_4 & B_5 & B_6 & B_7 \\ C_1 & C_2 & C_3 & C_4 & C_5 & C_6 & C_7 \\ D_1 & D_2 & D_3 & D_4 & D_5 & D_6 & D_7 \\ E_1 & E_2 & E_3 & E_4 & E_5 & E_6 & E_7 \\ F_1 & F_2 & F_3 & F_4 & F_5 & F_6 & F_7 \\ G_1 & G_2 & G_3 & G_4 & G_5 & G_6 & G_7 \end{pmatrix};$$

where,

$$\mathcal{A}(\omega) = [\mathcal{A}_1(\omega), \mathcal{A}_2(\omega), \mathcal{A}_3(\omega), \mathcal{A}_4(\omega), \mathcal{A}_5(\omega), \mathcal{A}_6(\omega), \mathcal{A}_7(\omega)]^T;$$

$$\mathcal{X}(\omega) = [\alpha_1 \mathcal{X}_1(\omega), \alpha_2 \mathcal{X}_2(\omega), \alpha_3 \mathcal{X}_3(\omega), \alpha_4 \mathcal{X}_4(\omega), \alpha_5 \mathcal{X}_5(\omega), \alpha_6 \mathcal{X}_6(\omega), \alpha_7 \mathcal{X}_7(\omega)]^T; \quad A_1(\omega) = i\omega;$$

$$A_2(\omega) = \frac{1}{N} \gamma S_1^*; \quad A_3(\omega) = \frac{1}{N} \delta S_1^*; \quad A_4(\omega) = A_5(\omega) = A_6(\omega) = A_7(\omega) = 0;$$

$$B_1(\omega) = -\frac{1}{N} \gamma S_2^*; \quad B_2(\omega) = i\omega; \quad B_3(\omega) = B_4(\omega) = B_5(\omega) = B_6(\omega) = B_7(\omega) = 0;$$

$$C_1(\omega) = C_2(\omega) = 0; \quad C_3(\omega) = i\omega; \quad C_4(\omega) = C_5(\omega) = C_6(\omega) = C_7(\omega) = 0;$$

$$D_1(\omega) = D_2(\omega) = D_3(\omega) = 0; \quad D_4(\omega) = i\omega; \quad D_5(\omega) = D_6(\omega) = D_7(\omega) = 0;$$

$$E_1(\omega) = E_2(\omega) = E_3(\omega) = E_4(\omega) = 0; \quad E_5(\omega) = i\omega; \quad E_6(\omega) = E_7(\omega) = 0;$$

$$F_1(\omega) = F_2(\omega) = F_3(\omega) = F_4(\omega) = F_5(\omega) = 0; \quad F_6(\omega) = i\omega; \quad F_7(\omega) = 0;$$

$$G_1(\omega) = G_2(\omega) = G_3(\omega) = G_4(\omega) = G_5(\omega) = G_6(\omega) = 0; \quad G_7(\omega) = i\omega;$$

Hence the solution of (2.17) is given by

$$\mathcal{A}(\omega) = K(\omega) \mathcal{X}(\omega), \quad \text{where} \quad K(\omega) = [M(\omega)]^{-1} \tag{2.18}$$

The solution components of (2.18) are given by

$$\mathcal{A}_i(\omega) = \sum_{j=1}^7 K_{ij}(\omega) \mathcal{X}_j(\omega); \quad i = 1, 2, 3, 4, 5, 6, 7 \tag{2.19}$$

The spectrum of $u_i, i = 1, 2, 3, 4, 5, 6, 7$ are given by

$$S_{u_i}(\omega) = \sum_{j=1}^7 \alpha_j |K_{ij}(\omega)|^2; \quad i = 1, 2, 3, 4, 5, 6, 7$$

Hence the intensities of fluctuations in the variable $u_i, i = 1, 2, 3, 4, 5, 6, 7$ are given by

$$\sigma_{u_i}^2 = \frac{1}{2\pi} \sum_{j=1}^7 \int_{-\infty}^{\infty} \alpha_j |K_{ij}(\omega)|^2 d\omega; \quad i = 1, 2, 3, 4, 5, 6, 7$$

That is, the variances of $u_i, i = 1, 2, 3, 4, 5, 6, 7$ are obtained as

$$\begin{aligned} \sigma_{u_1}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{11}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{12}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{13}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{14}(\omega)|^2 d\omega \right. \\ &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{15}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{16}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{17}(\omega)|^2 d\omega \right\} \\ \sigma_{u_2}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{21}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{22}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{23}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{24}(\omega)|^2 d\omega \right. \\ &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{25}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{26}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{27}(\omega)|^2 d\omega \right\} \end{aligned}$$

$$\begin{aligned}
 \sigma_{u_3}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{31}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{32}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{33}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{34}(\omega)|^2 d\omega \right. \\
 &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{35}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{36}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{37}(\omega)|^2 d\omega \right\} \\
 \sigma_{u_4}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{41}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{42}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{43}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{44}(\omega)|^2 d\omega \right. \\
 &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{45}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{46}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{47}(\omega)|^2 d\omega \right\} \\
 \sigma_{u_5}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{51}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{52}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{53}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{54}(\omega)|^2 d\omega \right. \\
 &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{55}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{56}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{57}(\omega)|^2 d\omega \right\} \\
 \sigma_{u_6}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{61}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{62}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{63}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{64}(\omega)|^2 d\omega \right. \\
 &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{65}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{66}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{67}(\omega)|^2 d\omega \right\} \\
 \sigma_{u_7}^2 &= \frac{1}{2\pi} \left\{ \int_{-\infty}^{\infty} \alpha_1 |B_{71}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_2 |B_{72}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_3 |B_{73}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_4 |B_{74}(\omega)|^2 d\omega \right. \\
 &\quad \left. + \int_{-\infty}^{\infty} \alpha_5 |B_{75}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_6 |B_{76}(\omega)|^2 d\omega + \int_{-\infty}^{\infty} \alpha_7 |B_{77}(\omega)|^2 d\omega \right\}
 \end{aligned} \tag{2.20}$$

where $B_{mn} = \frac{X_{mn} + iY_{mn}}{R(\omega) + iI(\omega)}$, $m, n = 1, 2, 3, 4, 5, 6, 7$

$$\begin{aligned}
 X_{11} &= -\omega^6; Y_{11} = 0; X_{12} = 0; Y_{12} = -\gamma S_1 \omega^5 / N; X_{13} = 0; Y_{13} = -\delta S_1 \omega^5 / N; \\
 X_{14} &= Y_{14} = X_{15} = Y_{15} = X_{16} = Y_{16} = X_{17} = Y_{17} = 0; \\
 X_{21} &= 0; Y_{21} = \gamma S_1 \omega^5 / N; X_{22} = -\omega^6; Y_{22} = 0; X_{23} = -\delta \gamma S_1^2 \omega^4 / N^2; Y_{23} = 0; \\
 X_{24} &= Y_{24} = X_{25} = Y_{25} = X_{26} = Y_{26} = X_{27} = Y_{27} = 0; \\
 X_{31} &= 0; Y_{31} = 0; X_{32} = 0; Y_{32} = 0; X_{33} = -\frac{\omega^4(N^2 \omega^2 - \gamma^2 S_1^2)}{N^2}; Y_{33} = 0; \\
 X_{34} &= Y_{34} = X_{35} = Y_{35} = X_{36} = Y_{36} = X_{37} = Y_{37} = 0; \\
 X_{41} &= Y_{41} = X_{42} = Y_{42} = X_{43} = Y_{43} = 0; X_{44} = -\frac{\omega^4(N^2 \omega^2 - \gamma^2 S_1^2)}{N^2}; Y_{44} = 0; \\
 X_{45} &= Y_{45} = X_{46} = Y_{46} = X_{47} = Y_{47} = 0; \\
 X_{51} &= Y_{51} = X_{52} = Y_{52} = X_{53} = Y_{53} = X_{54} = Y_{54} = 0; \\
 X_{55} &= -\frac{\omega^4(N^2 \omega^2 - \gamma^2 S_1^2)}{N^2}; Y_{55} = 0; X_{56} = Y_{56} = X_{57} = Y_{57} = 0; \\
 X_{61} &= Y_{61} = X_{62} = Y_{62} = X_{63} = Y_{63} = X_{64} = Y_{64} = X_{65} = Y_{65} = 0; \\
 X_{66} &= -\frac{\omega^4(N^2 \omega^2 - \gamma^2 S_1^2)}{N^2}; Y_{66} = 0; X_{67} = Y_{67} = 0; \\
 X_{71} &= Y_{71} = X_{72} = Y_{72} = X_{73} = Y_{73} = X_{74} = Y_{74} = X_{75} = Y_{75} = X_{76} = Y_{76} = 0;
 \end{aligned}$$

$$X_{77} = -\frac{\omega^4(N^2\omega^2 - \gamma^2S_1^2)}{N^2}; Y_{77} = 0;$$

Thus (2.20) becomes,

$$\begin{aligned} \sigma_{u_1}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{11}^2 + Y_{11}^2) + \alpha_2(X_{12}^2 + Y_{12}^2) + \alpha_3(X_{13}^2 + Y_{13}^2) + \alpha_4(X_{14}^2 + Y_{14}^2) + \alpha_5(X_{15}^2 + Y_{15}^2) \right. \\ &\quad \left. + \alpha_6(X_{16}^2 + Y_{16}^2) + \alpha_7(X_{17}^2 + Y_{17}^2) \right] d\omega \\ \sigma_{u_2}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{21}^2 + Y_{21}^2) + \alpha_2(X_{22}^2 + Y_{22}^2) + \alpha_3(X_{23}^2 + Y_{23}^2) + \alpha_4(X_{24}^2 + Y_{24}^2) + \alpha_5(X_{25}^2 + Y_{25}^2) \right. \\ &\quad \left. + \alpha_6(X_{26}^2 + Y_{26}^2) + \alpha_7(X_{27}^2 + Y_{27}^2) \right] d\omega \\ \sigma_{u_3}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{31}^2 + Y_{31}^2) + \alpha_2(X_{32}^2 + Y_{32}^2) + \alpha_3(X_{33}^2 + Y_{33}^2) + \alpha_4(X_{34}^2 + Y_{34}^2) + \alpha_5(X_{35}^2 + Y_{35}^2) \right. \\ &\quad \left. + \alpha_6(X_{36}^2 + Y_{36}^2) + \alpha_7(X_{37}^2 + Y_{37}^2) \right] d\omega \\ \sigma_{u_4}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{41}^2 + Y_{41}^2) + \alpha_2(X_{42}^2 + Y_{42}^2) + \alpha_3(X_{43}^2 + Y_{43}^2) + \alpha_4(X_{44}^2 + Y_{44}^2) + \alpha_5(X_{45}^2 + Y_{45}^2) \right. \\ &\quad \left. + \alpha_6(X_{46}^2 + Y_{46}^2) + \alpha_7(X_{47}^2 + Y_{47}^2) \right] d\omega \\ \sigma_{u_5}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{51}^2 + Y_{51}^2) + \alpha_2(X_{52}^2 + Y_{52}^2) + \alpha_3(X_{53}^2 + Y_{53}^2) + \alpha_4(X_{54}^2 + Y_{54}^2) + \alpha_5(X_{55}^2 + Y_{55}^2) \right. \\ &\quad \left. + \alpha_6(X_{56}^2 + Y_{56}^2) + \alpha_7(X_{57}^2 + Y_{57}^2) \right] d\omega \\ \sigma_{u_6}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{61}^2 + Y_{61}^2) + \alpha_2(X_{62}^2 + Y_{62}^2) + \alpha_3(X_{63}^2 + Y_{63}^2) + \alpha_4(X_{64}^2 + Y_{64}^2) + \alpha_5(X_{65}^2 + Y_{65}^2) \right. \\ &\quad \left. + \alpha_6(X_{66}^2 + Y_{66}^2) + \alpha_7(X_{67}^2 + Y_{67}^2) \right] d\omega \\ \sigma_{u_7}^2 &= \frac{1}{2\pi} \int_{-\infty}^{\infty} \frac{1}{R^2(\omega) + I^2(\omega)} \left[\alpha_1(X_{71}^2 + Y_{71}^2) + \alpha_2(X_{72}^2 + Y_{72}^2) + \alpha_3(X_{73}^2 + Y_{73}^2) + \alpha_4(X_{74}^2 + Y_{74}^2) + \alpha_5(X_{75}^2 + Y_{75}^2) \right. \\ &\quad \left. + \alpha_6(X_{76}^2 + Y_{76}^2) + \alpha_7(X_{77}^2 + Y_{77}^2) \right] d\omega \end{aligned}$$

where $|M(\omega)| = R(\omega) + iI(\omega)$; $R(\omega) = 0$; $I(\omega) = -\frac{\omega^5}{N^2}(N^2\omega^2 - \gamma^2S_1^2)$

If we consider the noise effect on any one of the classes, and if we want know the characteristics of the system (1) with either $\alpha_3 = 0$ or $\alpha_4 = 0$ or $\alpha_5 = 0$ or $\alpha_6 = 0$ or $\alpha_7 = 0$ then the population variances are:

If $\alpha_1 = \alpha_2 = \alpha_3 = \alpha_4 = \alpha_5 = \alpha_6 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_2}^2 = \sigma_{u_3}^2 = \sigma_{u_4}^2 = \sigma_{u_5}^2 = \sigma_{u_6}^2 = 0; \sigma_{u_7}^2 = \frac{\alpha_7}{2\pi} \int_{-\infty}^{\infty} \frac{X_{77}^2}{R^2(\omega) + I^2(\omega)} d\omega;$$

If $\alpha_1 = \alpha_2 = \alpha_3 = \alpha_4 = \alpha_5 = \alpha_7 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_2}^2 = \sigma_{u_3}^2 = \sigma_{u_4}^2 = \sigma_{u_5}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_6}^2 = \frac{\alpha_6}{2\pi} \int_{-\infty}^{\infty} \frac{X_{66}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

If $\alpha_1 = \alpha_2 = \alpha_3 = \alpha_4 = \alpha_6 = \alpha_7 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_2}^2 = \sigma_{u_3}^2 = \sigma_{u_4}^2 = \sigma_{u_6}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_5}^2 = \frac{\alpha_5}{2\pi} \int_{-\infty}^{\infty} \frac{X_{55}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

If $\alpha_1 = \alpha_2 = \alpha_3 = \alpha_5 = \alpha_6 = \alpha_7 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_2}^2 = \sigma_{u_3}^2 = \sigma_{u_5}^2 = \sigma_{u_6}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_4}^2 = \frac{\alpha_4}{2\pi} \int_{-\infty}^{\infty} \frac{X_{44}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

If $\alpha_1 = \alpha_2 = \alpha_4 = \alpha_5 = \alpha_6 = \alpha_7 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_2}^2 = \sigma_{u_4}^2 = \sigma_{u_5}^2 = \sigma_{u_6}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_3}^2 = \frac{\alpha_3}{2\pi} \int_{-\infty}^{\infty} \frac{X_{33}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

If $\alpha_1 = \alpha_3 = \alpha_4 = \alpha_5 = \alpha_6 = \alpha_7 = 0$ then,

$$\sigma_{u_1}^2 = \sigma_{u_3}^2 = \sigma_{u_4}^2 = \sigma_{u_5}^2 = \sigma_{u_6}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_2}^2 = \frac{\alpha_2}{2\pi} \int_{-\infty}^{\infty} \frac{X_{22}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

If $\alpha_2 = \alpha_3 = \alpha_4 = \alpha_5 = \alpha_6 = \alpha_7 = 0$ then,

$$\sigma_{u_2}^2 = \sigma_{u_3}^2 = \sigma_{u_4}^2 = \sigma_{u_5}^2 = \sigma_{u_6}^2 = \sigma_{u_7}^2 = 0; \sigma_{u_1}^2 = \frac{\alpha_1}{2\pi} \int_{-\infty}^{\infty} \frac{X_{11}^2}{R^2(\omega) + I^2(\omega)} d\omega$$

As a result the population variances indicate the steadiness of inhabitants for minor values of mean square fluctuations, while the greater values of population variances show the instability of the populations.

7. Conclusion with Numerical Simulations

In this article we have focused on the dynamical behaviour of the HBV model. It is found that the disease free equilibrium is globally asymptotically stable for $R_0 < 1$ and chronic individuals persist in the society only when asymptomatic individuals exist.

The numerical simulation using hypothetical set of parameter values suggests that the system is stable which is vividly depicted in Figure 2. Figure 3 and Figure 4 illustrate that by controlling the rate of propagation to the chronic class (k) we can reduce the hepatocellular carcinoma developed individuals and at the same time able to increase the recovered individuals. In other words, the propagation of the disease can be controlled by reducing number of chronically infected individuals in the society and also by preventing their exposures with the susceptible individuals. By reducing disease induced death rate (ξ) using treatment, individuals can be able to survive with prolonged illness caused by carcinoma which is depicted in Figure 5 also.

To investigate the effect of environmental noise on the deterministic model numerically, stochastic perturbations are applied on the system (1) with respect to white noise around its positive equilibrium. From Figure 6a and Figure 6b we remark that with the various intensities of noise up-to certain tolerance limit, stochastic effect plays an important role on the size of epidemic and the trajectories ultimately converge to stability instead of initial oscillation to the system. From the stochastic analysis it is observed the steadiness of inhabitants for minor values of mean square fluctuations, while the greater values of population variances indicate its instability. In brief, there is no fundamental difference in dynamics rather than the oscillation for the randomly fluctuating environment on the system by additive white noises and we can be able to check the fluctuation of the disease by controlling the strength of the noises.

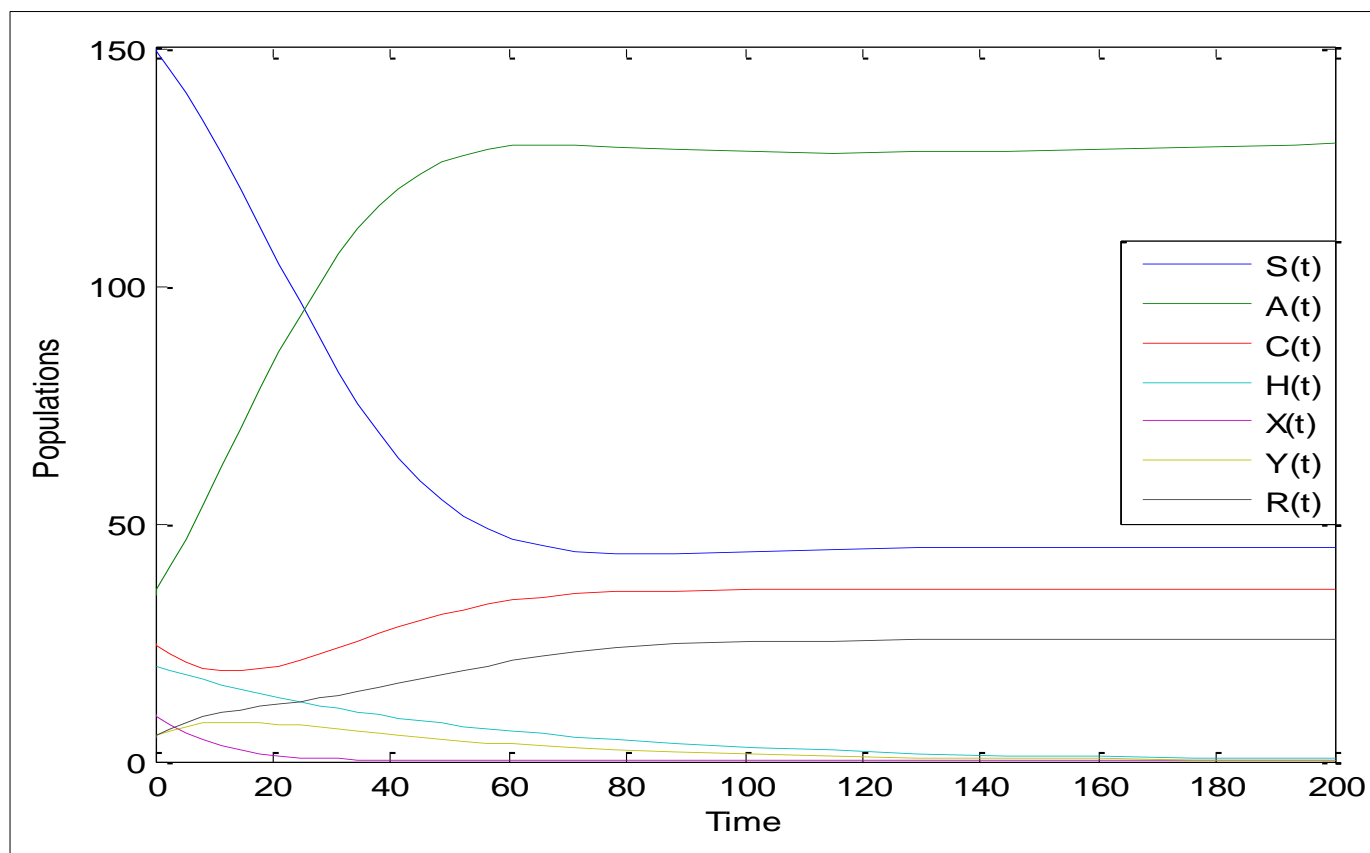


Fig 2: The figure illustrates the trajectories of the system for $N = 200, b = 1, \gamma = .08, \delta = .05, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = .0001, k = .02, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08$

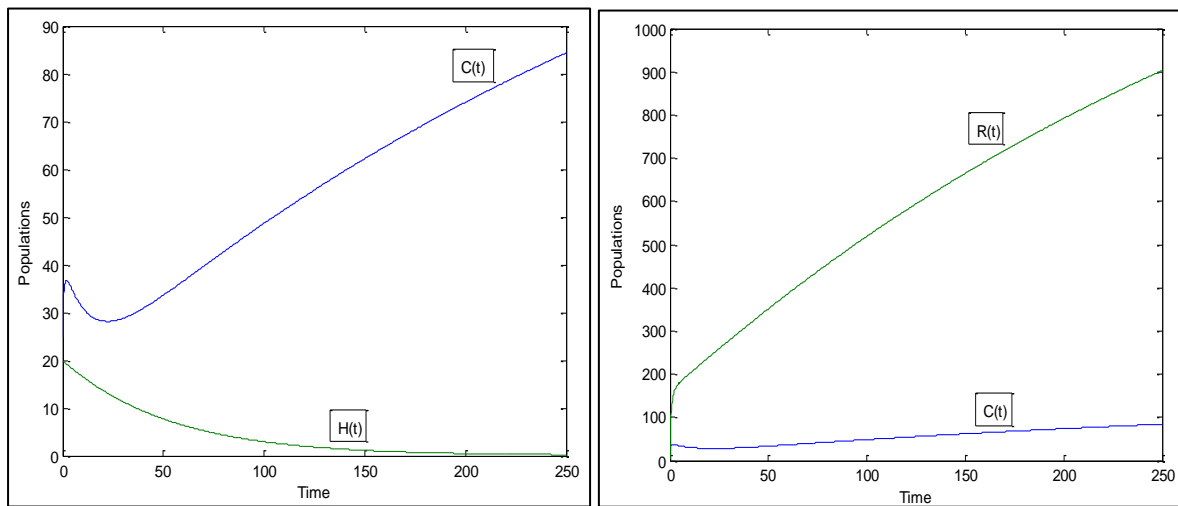


Fig 3: The figure illustrates the trajectories of the system for $N = 200, b = 5, \gamma = 8, \delta = 5, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = 10, k = 1, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08$

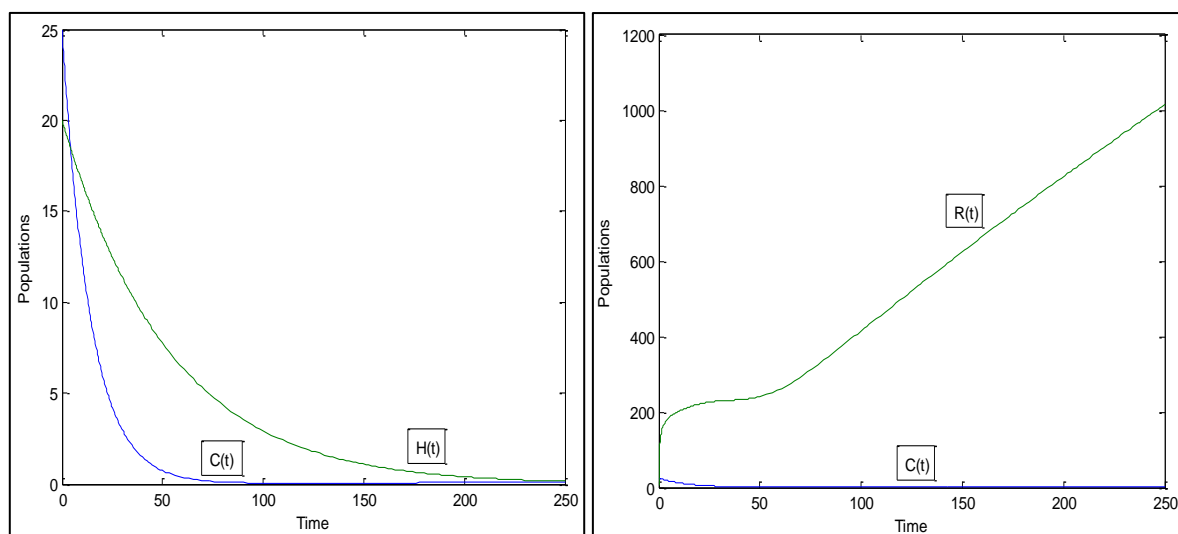


Fig 4: The figure illustrates the trajectories of the system for $N = 200, b = 5, \gamma = 8, \delta = 5, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = 10, k = .001, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08$

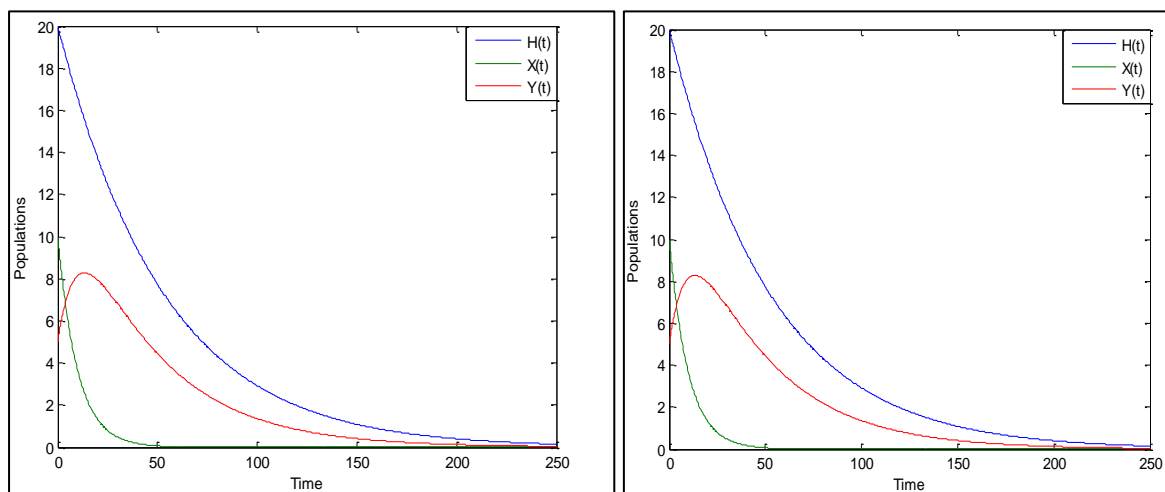


Fig 5: The figure illustrates the trajectories of the system for $N = 200, b = 5, \gamma = 8, \delta = 5, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = 10, k = .001, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08$ with $\xi = .02$ for the left figure and $\xi = .002$ for the right figure.

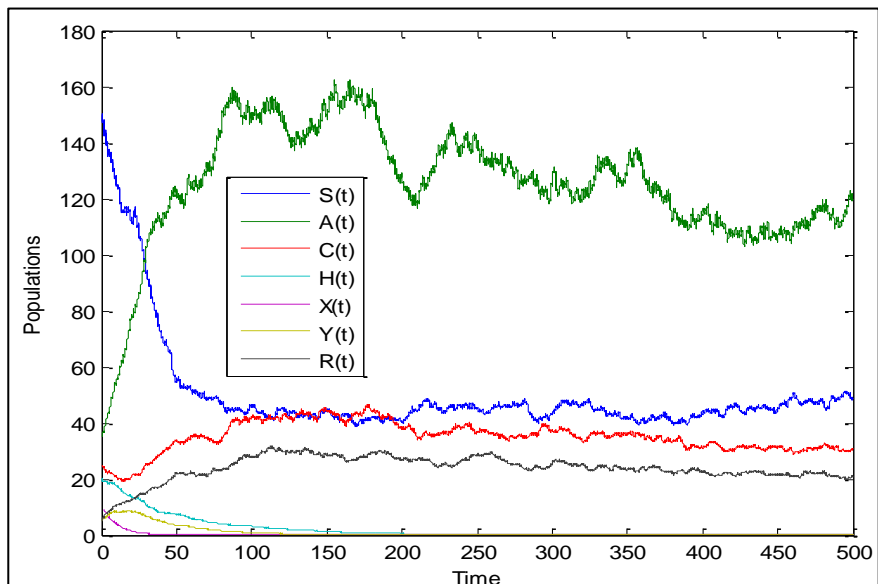


Fig 6a: The figure illustrates the trajectories of the system for $N = 200, b = 1, \gamma = .08, \delta = .05, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = .0001, k = .02, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08, s = .5$.

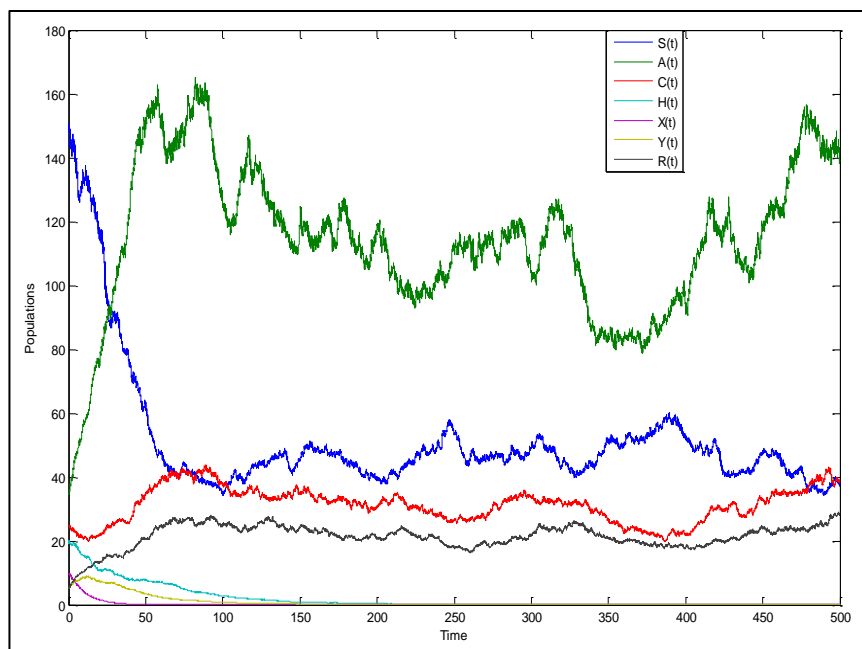


Fig 6b: The figure illustrates the trajectories of the system for $N = 200, b = 1, \gamma = .08, \delta = .05, \mu = .001, \tau = .01, \psi = .07, \sigma = .003, \alpha = .0001, k = .02, \varepsilon = .0002, \beta = .05, \xi = .02, \phi = .03, \eta = .04, \rho = .08, s = 1$.

7. References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V *et al.*, Global and regional mortality from 235 causes of death for 20 age groups in and 2010: a systematic analysis for the Global Burden of Disease Study 2010, *Lancet*. 1990; 380:2095-2128.
2. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures, *J Viral Hepat.*, 2004; 11(2):97-107.
3. Weekly epidemiological record. World Health Organization. 2009; 40(84):405-420.
4. Mast EE, Margolis HS, Fiore AE *et al.* A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep*. 2005; 54(RR-16):1-31.
5. WHO Media Centre, Fact sheet N°204.
6. Muhammad AK, Islam S, Muhammad A, Haq Z. Transmission Model of Hepatitis B Virus with the Migration Effect, *BioMed Research International*. 2013, 1-10. Article ID 150681.
7. Kamyad AV, Akbari R, Heydari AA, Heydari A., Mathematical Modeling of Transmission Dynamics and Optimal Control of Vaccination and Treatment for Hepatitis B Virus, *Computational and Mathematical Methods in Medicine*, 2014, 1-15, Article ID 475451.

8. Long C., Qi H., Huang S.H., A Dynamic Model for the Hepatitis B Virus Infection, *Systemics, Cybernetics and Informatics*. 2007; 5(1):1-5.
9. Kimbir AR, Aboiyar T, Abu O, Onah ES. Simulation of A Mathematical Model Of Hepatitis B Virus Transmission Dynamics In The Presence Of Vaccination And Treatment, *Mathematical Theory and Modeling*. 2014; 4(12):44-59.
10. Zou L, Zhang W, Ruan S. Modeling the transmission dynamics and control of hepatitis B virus in China, *Journal of Theoretical Biology*. 2010; 262:330-338.
11. Zhang J, Zhang S. Application and Optimal Control for an HBV Model with Vaccination and Treatment, *Discrete Dynamics in Nature and Society*, 2018. Article ID 2076983, 13 pages, Hindawi.
12. Liang TJ. Hepatitis B: The Virus and Disease, *Hepatology*, 200949 (5 Suppl): S13–S21,.
13. Castillo-Chavez C, Feng Z, Huang W. On the computation of R_0 and its role on global stability, *Mathematical Approaches for Emerging and Reemerging Infectious Diseases*, 2001. IMA Vol. Math. Appl. Springer, New York.
14. Nisbet RM, Gurney WSC. *Modelling Fluctuating Populations*, John Wiley, New York, 1982.
15. Carletti M. Numerical solution of stochastic differential problems in the biosciences, *J Comput Appl Math*. 2006; 185:422-440.