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Sensitivity Analysis of the Mathematical Model Parameters of the HBV Disease Transmission Dynamics with Controls

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Abstract

In this research paper, the sensitivity analysis of the existence of Hepatitis B virus infection with respect to the parameters of the model of HBV infection with controls were carried out. The basic reproduction number R_0 was calculated and consequently used to carry out the sensitivity analysis using mathcad. The result showed that π (recruitment) and β (contact rate for HBV infectious individuals with the susceptible individuals) with sensitivity index of $+1.00$ each are the most sensitive parameters that affect the transmission dynamics of HBV infection in the population. These parameters enhances the infectivity of the disease, and so must be targeted seriously in the control strategy to ensure that the disease is wiped out totally.

Keywords: Sensitivity Analysis, Hepatitis B Virus, parameters, Basic Reproduction Number, Infectivity, Transmission dynamics, Mathcad.

1.0 Introduction

Hepatitis means inflammation of the Liver. Human hepatitis B is the prototype virus of the hepadna virus family and causes serum hepatitis. HBV has a diameter of about 40nm.The hepatitis B Virus (HBV) is the only hepadna virus causing infection in humans. The swelling and irritation associated with inflammation is the body's attempt to heal itself and it occurs whenever there is an injury or illness in the body. The inflammation of the liver can cause the liver not to work properly, which is of serious concern when consideration is given to the job that the liver performs every day. The liver is responsible for removing harmful substances from the blood, aiding in food digestion and storing nutrients in the body.

Hepatitis B is one of the serious infectious diseases which threaten the global human health, and has become an important social and public health issue [1]. Chronic hepatitis B virus (CHBV) infection can cause liver inflammation and fibrosis, and severe cases may develop into cirrhosis or liver cancer. HBV has infected nearly 2,000,000,000 people around the world, and no less than 240,000,000 persons become lifelong infected of HBV [2, 1]. A chronic infection in liver, which probably develops into cirrhosis of the liver or liver cancer afterwards, can also be given rise to by HBV. Because of the acute or chronic effects of hepatitis B, approximately 780,000 people die every year [1,2,3].

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV)[4, 3]. It is a major global health problem but hepatitis C and hepatitis B (with HDV) are the mostserious types of viral hepatitis in the world [5]. Originally known as "serum hepatitis", the disease has caused epidemics in parts of Asia andAfrica, and it is endemic in China [6, 3]. About a third of the world population has been infected atone point in their lives, including 350 million who are chronic carriers which causes 620,000deaths worldwide each year [7, 8].Hepatitis B virus is transmitted between people by direct blood-to-blood contact or semen andvaginal fluid of an infected person[9]. Modes of transmission are the same as those for thehuman immunodeficiency virus (HIV), but the hepatitis B virus is 50 to 100 times more infectious[10]. Unlike HIV, the hepatitis B virus can survive outside the body for at least seven days.During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine [11].

Hepatitis, inflammation of the liver is caused by viruses, bacterial infections, or continuousexposure to alcohol, drugs, or toxic chemicals, such as those found in aerosol sprays and paintthinners [12]. Inflammation is the painful, red swelling that

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result when tissues of the body becomeinjured or infected [6]. In clinical sciences, hepatitis is divided into three categories, namely, acutehepatitis, chronic hepatitis and fulminant hepatitis. Inflammation can cause organs notto workproperly. Hepatitis can also result from an autoimmune disorder, in which the body mistakenlysends disease-fighting cells to attack its own healthy tissue, in this case the liver[13]. No matter what its cause, hepatitis reduces the liver'sability to perform life-preserving functions[4].

The other important function of liver is producingcritical hormones. When we speak of viral hepatitis, we usually are referring to hepatitis caused by a fewspecific viruses that primarily attack the liver [3]. There are several hepatitis viruses; they have beennamed types A, B, C, D, E, F even though not confirmed, and G [14, 15]. As our knowledge ofhepatitis viruses grows, it is likely that this alphabetical list will become longer [16]. The mostcommon hepatitis viruses are types A, B, and C [17]. In the natural history of HBV infection, it is estimated that 10% to 33% of those who developpersistent infection end up with chronic hepatitis of which 20% to 50% may develop livercirrhosis [3]. Hepatitis B is considered an important public health problem necessitating highpriority strategies for control[3]. An estimated worldwide carrier of hepatitis Bvirus is 350 million, with an estimated 50 million chronic carriers of HBV in Africa[3].

Sensitivity Analysis is defined as the study of how the variation in the output of a model (numerical or otherwise) can be attributed to different variations in the input of the model [18].There are more than a dozen ways of conducting sensitivity analysis, all resulting in a slightly different sensitivity ranking [19]. The normalized forward sensitivity index also called elasticity is the backbone of nearly all other sensitivity analysis techniques [19]. The normalized forward sensitivity index also called elasticity is computationally efficient [20]. The basic reproduction number, R_0 is a measure of the potential for disease spread in a population, and is inarguably 'one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory' [21]. It represents the average number of secondary cases generated by an infected individual if introduced into a susceptible population with no immunity to the disease in the absence of interventions to control the infection [22,23]. Sensitivity analysis is indispensable in order to determine the relative importance of the different parameters responsible for the transmission and prevalence of the disease in the population [22].

In this research paper, we built a mathematical model for the HBV infection with controls (enlightenment, condom use, vaccine and therapy). Equilibrium analysis on the modeled equations were carried out. Furthermore, basic reproduction number R_0 was calculated. Consequently, the sensitivity analysis of the existence of Hepatitis B virus infection with respect to the parameters of the model of HBV infection with controls were carried out.

2.0 Model formulation for HBV

2.1 Assumptions of the Model:

The model is based on the following assumptions:

1. The individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state
2. The population size in a compartment varies with respect to time.
3. The population mixes homogeneously. That is, all susceptible individuals are equally likely to be infected by infectious individuals if they come in contact with one another.
4. The infection does not confer immunity to the recovered individuals and so they can go back to the susceptible class at any given time.
5. The individuals in each compartment have equal natural death rate given as μ
6. The gain in the infectious class is at a rate proportional to the number of infectious and susceptible individuals, that is, βSI, where $\beta > 0$ is a contact parameter (effective contact rate).The susceptible are lost at the same rate
7. The rate of removal of infectious to the recovered or removed class is proportional to the number of infectious individuals.

8 Individuals that enter into the population will either go into the susceptible class or into the infectious class depending on their epidemiological condition as at the time of entering.

2.2 Model Variables:

The following variables will be used in this model:

$\boldsymbol{S}$: The number of susceptible individuals.

$\boldsymbol{E}$: The number of exposed individuals.

$\boldsymbol{I}$: The number of infectious individuals.

$\boldsymbol{R}$: The number of individuals who have been treated and have recovered from the infection.

$\boldsymbol{E_T}$: The number of exposed individuals who are receiving treatment.

$\boldsymbol{I_T}$: The number of infectious individuals who are receiving treatment.

$\boldsymbol{I_N}$: The number of infectious individuals who are not receiving treatment.

2.3 Model Parameters:

We shall use the following parameters in this model, they are:

π: The number of people that enter into the population or the number of individuals that enter into the susceptible class(recruitment).
β : Contact rate for HBV infectious individuals with the susceptible individuals. i.e., the rate at which susceptible individuals who had contact with the infected become exposed to HBV.
τ: The rate at which latently infected individuals become infectious (actively infected).
ω: The rate at which exposed individuals enter the exposed and treated class (E_T).
ρ_2: The rate at which infectious individuals enter into the infectious and treated class (I_T).
α: The rate at which infectious and treated individuals go back to exposed class (E)
ρ_1: The rate at which infectious individuals enter into the class of infected and not treated.
λ: The rate at which infectious and treated individuals recover from HBV (the rate at which infectious and treated individuals move to the recovered class R).
ϕ: The rate at which recovered individuals become susceptible to HBV again.
δ: HBV-induced mortality/death rate for the class of infectious and treated individuals.
δ_1: HBV-induced mortality/death rate for the class of infectious and not treated individuals
μ: The natural mortality/death rate.
$\psi(1+\varphi)$: The rate at which exposed and treated individuals recover.
φ: Infectivity control; which include enlightenment, vaccine and the use of condom.
θ: The number of individuals already infected with HBV that goes into the population
ψ: Cure rate

2.4 Model Description:

Base on the standard SEIR model, the population is partitioned into seven compartments or classes namely: Susceptible(S), Exposed(E), Infectious(I), Exposed and Treated(E_T), Infectious and Treated(I_T), Infectious and not Treated(I_N) and Recovered(R) Compartments.

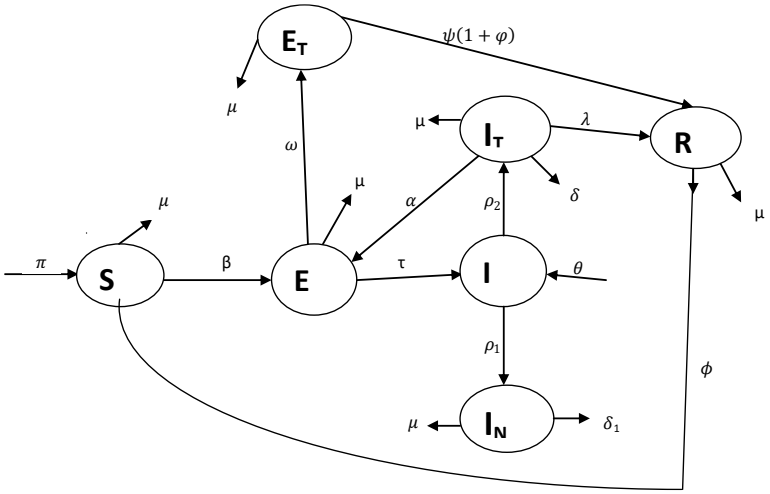

Figure 1: Flow Diagram of HBV Transmission with controls

Equations Governing the Model:

$$\frac{dS}{dt} = \pi + \phi R - \beta SI - \mu S \quad (1.1)$$
$$\frac{dE}{dt} = \beta SI + \alpha I_T - \omega E - \tau E - \mu E \quad (1.2)$$
$$\frac{dE_T}{dt} = \omega E - \psi(1+\varphi)E_T - \mu E_T \quad (1.3)$$
$$\frac{dI}{dt} = \tau E + \theta I - \rho_1 I - \rho_2 I \quad (1.4)$$
$$\frac{dI_N}{dt} = \rho_1 I - \mu I_N - \delta_1 I_N \quad (1.5)$$
$$\frac{dI_T}{dt} = \rho_2 I - \alpha I_T - \lambda I_T - \mu I_T - \delta I_T \quad (1.6)$$
$$\frac{dR}{dt} = \lambda I_T + \psi(1+\varphi)E_T - \phi R - \mu R \quad (1.7)$$
$$N = S + E + E_T + I_N + I_T + R \quad (1.8)$$

Susceptible individuals acquire HBV infection following effective contact with individuals infected with HBV (i.e., those in the $E, I_N and I_T$ classes) at a rateβ, given by

$\beta = \frac{\chi_B(E+\mu_1 I_N+\mu_2 I_T)}{N}$; $\quad N = S + E + I_N + I_T$

where χ_B is the effective contact rate for HBV transmission. Further, the modification parameters $\mu_1 \geq 1$ $and \mu_2 < 1$ account for the relative infectiousness of individuals in the I_N and I_T classes in comparison to those in the E class. That is individuals in the I_N class are more infectious than those in the E class (because of their higher viral load), and likewise, I_T are less infectious than those in I_N class (because the use of treatment significantly reduces the viral load in those treated).

3.0 Analysis of the Model:

3.1 Equilibrium Solutions:

Let $E: (S, E, E_T, I, I_N, I_T, R)$ be the equilibrium point of the system described by the equations (1.1) - (1.8). At the equilibrium state, we have that; $\dot{S} = \dot{E} = \dot{E}_T = \dot{I} = \dot{I}_N = \dot{I}_T = R = 0$. That is,

$$\pi + \phi R - \beta SI - \mu S = 0 \quad (1.9)$$
$$\beta SI + \alpha I_T - \omega E - \tau E - \mu E = 0 \quad (1.10)$$
$$\omega E - \psi(1+\varphi)E_T - \mu E_T = 0 \quad (1.11)$$
$$\tau E + \theta I - \rho_1 I - \rho_2 I = 0 \quad (1.12)$$
$$\rho_1 I - \mu I_N - \delta_1 I_N = 0 \quad (1.13)$$
$$\rho_2 I - \alpha I_T - \lambda I_T - \mu I_T - \delta I_T = 0 \quad (1.14)$$
$$\lambda I_T + \psi(1+\varphi)E_T - \phi R - \mu R = 0 \quad (1.15)$$

In order to obtain the disease-free equilibrium state, we shall solve equations (1.9) – (1.15) simultaneously

3.2 The Disease-free Equilibrium (DFE)

The disease-free equilibrium state is the state of total absence of the disease.

Let $E^0: (S^*, E^*, E_T^*, I^*, I_N^*, I_T^*, R^*)$ be the disease-free equilibrium state. At the disease-free equilibrium state, we have that the exposed, the exposed and treated, the infectious, the infectious and treated as well as the infectious and not treated classes must be equal to zero.

That is, for disease-free equilibrium state, we must have that

$$E = E_T = I = I_N = I_T = 0 \quad (1.16)$$

Now by substituting the value of equation (1.16) into equations (1.9) – (1.15) and solving simultaneously, we obtain the following results;

From equation (1.15);

$-\mu R - \phi R = 0$ This implies that

$-\mu R = \phi R$

$(\mu - \phi)R = 0 \implies R = 0$

Hence, equation (1.9) becomes;

$$\pi - \mu S = 0 \quad (1.17)$$

This implies that $\pi - \mu S = 0$

Hence $\pi = \mu S$.

$$\therefore S = \frac{\pi}{\mu} \quad (1.18)$$

Therefore the disease- free equilibrium state of the model is thus;

$$E^0: (S^*, E^*, E_T^*, I^*, I_N^*, I_T^*, R^*) = \left(\frac{\pi}{\mu}, 0,0,0,0,0,0\right) \in R^7 \quad (1.19)$$

3.3 Basic Reproduction Number (R_0)

Recall that the disease-free equilibrium state of the model was calculated thus;

$$E^0: (S^*, E^*, E_T^*, I^*, I_N^*, I_T^*, R^*) = \left(\frac{\pi}{\mu}, 0,0,0,0,0,0\right) \in R^7 \quad (1.20)$$

We shall use the method of next-generation matrix G, which consist of two parts; F and V^{-1}

Where $F = \left[\frac{\partial F_i(E^0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(E^0)}{\partial x_j}\right]$ (1.21)

The F_i are the new infections, while the V_i are transfers of infections from one component to another [24, 25], E^0 is the disease-free equilibrium state.

R_0 is the dominant eigenvalue of the matrix $G = FV^{-1}$ [24, 25]

To calculate the basic reproduction number by using a next-generation matrix, the whole population is divided into n compartments in which there are $m < n$ infected compartments. In our model among seven compartments we have five infected compartments.

Let $x_i, i = 1,2,3, \dots, m$ be the numbers of infected individuals in the i^{th} infected compartment at time t. Let $F_i(x)$ be the rate of appearance of new infections in compartment. Let $V_i(x)$ be the difference between rates of transfer of individuals between

i^{th} compartments; $V_i^+(x)$ be the rate of transfer of individuals into i^{th} compartment by all other means, $V_i^-(x)$ be the rate of transfer of individuals out of i^{th} compartment by all other means.

$\frac{dx_i}{dt} = F_i(x) - V_i(x);$ (1.22)

where $V_i(x) = \{V_i^-(x) - V_i^+(x)\}$

The above equation (1.22) can be written as

$\frac{dx_i}{dt} = F(x) - V(x).$

Where; $F(x) = \{F_1(x), F_2(x), \dots, F_m(x)\}^T$

$V(x) = \{V_1(x), V_2(x), \dots, V_m(x)\}^T.$

4.0 Model Equations

$$\left.\begin{aligned} \frac{dE}{dt} &= \beta SI + \alpha I_T - (\omega + \tau + \mu)E \\ \frac{dE_T}{dt} &= \omega E - \{\mu + \psi(1+\varphi)\}E_T \\ \frac{dI}{dt} &= \tau E + (\theta - \rho_2 - \rho_1)I \\ \frac{dI_N}{dt} &= \rho_1 I - (\mu + \delta_1)I_N \\ \frac{dI_T}{dt} &= \rho_2 I - (\alpha + \mu + \delta + \lambda)I_T \end{aligned}\right\} \quad (1.23)$$

From equation (1.23), we have our Fas;

$F = (F_1, F_2, F_3, F_4, F_5)^T.$

$\Rightarrow F = (\beta SI, 0,0,0,0)^T.$

$$\therefore F_i = \begin{pmatrix} \beta SI \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \quad (1.24)$$

$V = (V_1, V_2, V_3, V_4, V_5)^T.$ (1.25)

$\Rightarrow V = \{-\alpha I_T + (\omega + \tau + \mu)E, -\omega E + \{\mu + \psi(1+\varphi)\}E_T, -\tau E - (\theta - \rho_2 - \rho_1)I, \rho_1 I - (\mu + \delta_1)I_N, -\rho_2 I + (\alpha + \mu + \delta + \lambda)I_T\}^T$

$$\therefore V_i = \begin{bmatrix} -\alpha I_T + (\omega + \tau + \mu)E \\ -\omega E + \{\mu + \psi(1+\varphi)\}E_T \\ -\tau E - (\theta - \rho_2 - \rho_1)I \\ -\rho_1 I + (\mu + \delta_1)I_N \\ -\rho_2 I + (\alpha + \mu + \delta + \lambda)I_T \end{bmatrix}. \quad (1.26)$$

We differentiate F_i and V_i with respect to $E, E_T, I, I_N and I_T$ and get $F and V$ respectively as shown below;

$$F = \left[\frac{\partial F_i(E^0)}{\partial x_j}\right] = \begin{bmatrix} \frac{\partial F_1}{\partial E} & \frac{\partial F_1}{\partial E_T} & \frac{\partial F_1}{\partial I} & \frac{\partial F_1}{\partial I_N} & \frac{\partial F_1}{\partial I_T} \\ \frac{\partial F_2}{\partial E} & \frac{\partial F_2}{\partial E_T} & \frac{\partial F_2}{\partial I} & \frac{\partial F_2}{\partial I_N} & \frac{\partial F_2}{\partial I_T} \\ \frac{\partial F_3}{\partial E} & \frac{\partial F_3}{\partial E_T} & \frac{\partial F_3}{\partial I} & \frac{\partial F_3}{\partial I_N} & \frac{\partial F_3}{\partial I_T} \\ \frac{\partial F_4}{\partial E} & \frac{\partial F_4}{\partial E_T} & \frac{\partial F_4}{\partial I} & \frac{\partial F_4}{\partial I_N} & \frac{\partial F_4}{\partial I_T} \\ \frac{\partial F_5}{\partial E} & \frac{\partial F_5}{\partial E_T} & \frac{\partial F_5}{\partial I} & \frac{\partial F_5}{\partial I_N} & \frac{\partial F_5}{\partial I_T} \end{bmatrix} = \begin{bmatrix} 0 & 0 & \beta\frac{\pi}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \quad (1.27)$$

Similarly, we get the value of V as follows;

$$V = \left[\frac{\partial V_i(E^0)}{\partial x_j}\right] = \begin{bmatrix} \frac{\partial V_1}{\partial E} & \frac{\partial V_1}{\partial E_T} & \frac{\partial V_1}{\partial I} & \frac{\partial V_1}{\partial I_N} & \frac{\partial V_1}{\partial I_T} \\ \frac{\partial V_2}{\partial E} & \frac{\partial V_2}{\partial E_T} & \frac{\partial V_2}{\partial I} & \frac{\partial V_2}{\partial I_N} & \frac{\partial V_2}{\partial I_T} \\ \frac{\partial V_3}{\partial E} & \frac{\partial V_3}{\partial E_T} & \frac{\partial V_3}{\partial I} & \frac{\partial V_3}{\partial I_N} & \frac{\partial V_3}{\partial I_T} \\ \frac{\partial V_4}{\partial E} & \frac{\partial V_4}{\partial E_T} & \frac{\partial V_4}{\partial I} & \frac{\partial V_4}{\partial I_N} & \frac{\partial V_4}{\partial I_T} \\ \frac{\partial V_5}{\partial E} & \frac{\partial V_5}{\partial E_T} & \frac{\partial V_5}{\partial I} & \frac{\partial V_5}{\partial I_N} & \frac{\partial V_5}{\partial I_T} \end{bmatrix}$$

$$V = \begin{bmatrix} (\omega+\tau+\mu) & 0 & 0 & 0 & -\alpha \\ -\omega\{\mu+\psi(1+\varphi)\} & 0 & 0 & 0 & \\ -\tau & 0 & -(\theta-\rho_2-\rho_1) & 0 & 0 \\ 0 & 0 & -\rho_1 & (\mu+\delta_1) & 0 \\ 0 & 0 & -\rho_2 & 0 & (\alpha+\mu+\delta+\lambda) \end{bmatrix}$$

Let

$M_1 := \omega + \tau + \mu$

$M_2 := \mu + \psi\cdot(1 + \Phi)$

$M_3 := \rho_2 + \rho_1 - \theta$

$M_4 := \mu + \delta 1$

$M_5 := \alpha + \mu + \delta + \lambda$

Therefore we have that; $V =$

$$\begin{pmatrix} M_1 & 0 & 0 & 0 & -\alpha \\ -\omega & M_2 & 0 & 0 & 0 \\ -\tau & 0 & M_3 & 0 & 0 \\ 0 & 0 & -\rho_1 & M_4 & 0 \\ 0 & 0 & -\rho_2 & 0 & M_5 \end{pmatrix}$$

Consequently, we have the inverse of V as shown below;

$V^{-1} =.$

$$\begin{pmatrix} M_1 & 0 & 0 & 0 & -\alpha \\ -\omega & M_2 & 0 & 0 & 0 \\ -\tau & 0 & M_3 & 0 & 0 \\ 0 & 0 & -\rho_1 & M_4 & 0 \\ 0 & 0 & -\rho_2 & 0 & M_5 \end{pmatrix}^{-1}$$

$\Rightarrow$

$$\begin{pmatrix} -\frac{M_3 \cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot M_3}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \\ -\frac{\omega\cdot M_3\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} & \frac{1}{M_2} & -\frac{\alpha\cdot\omega\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot\omega\cdot M_3}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} \\ -\frac{\tau\cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{M_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\tau\cdot\alpha}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \\ -\frac{\tau\cdot\rho_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} & 0 & -\frac{\rho_1\cdot M_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} & \frac{1}{M_4} & -\frac{\tau\cdot\alpha\cdot\rho_1}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} \\ -\frac{\tau\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\rho_2\cdot M_1}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{M_1\cdot M_3}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \end{pmatrix}$$

Now $FV^{-1} =$

$$\begin{pmatrix} 0 & 0 & \beta\cdot\frac{\pi}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \cdot \begin{pmatrix} -\frac{M_3 \cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot M_3}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \\ -\frac{\omega\cdot M_3\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} & \frac{1}{M_2} & -\frac{\alpha\cdot\omega\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} & 0 & -\frac{\alpha\cdot\omega\cdot M_3}{\tau\cdot\alpha\cdot\rho_2\cdot M_2 - M_1\cdot M_2\cdot M_3\cdot M_5} \\ -\frac{\tau\cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{M_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\tau\cdot\alpha}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \\ -\frac{\tau\cdot\rho_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} & 0 & -\frac{\rho_1\cdot M_1\cdot M_5}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} & \frac{1}{M_4} & -\frac{\tau\cdot\alpha\cdot\rho_1}{\tau\cdot\alpha\cdot\rho_2\cdot M_4 - M_1\cdot M_3\cdot M_4\cdot M_5} \\ -\frac{\tau\cdot\rho_2}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{\rho_2\cdot M_1}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} & 0 & -\frac{M_1\cdot M_3}{\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5} \end{pmatrix}$$

$\Rightarrow$

$$\begin{bmatrix} -\frac{\pi\cdot\tau\cdot\beta\cdot M_5}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} & 0 & -\frac{\pi\cdot\beta\cdot M_1\cdot M_5}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} & 0 & -\frac{\pi\cdot\tau\cdot\beta\cdot\alpha}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

We now obtain the characteristic equation $|FV^{-1} - I\Gamma| = 0$ as follows;

$$\left|\begin{bmatrix} -\Gamma - \frac{\pi\cdot\tau\cdot\beta\cdot M_5}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} & 0 & -\frac{\pi\cdot\beta\cdot M_1\cdot M_5}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} & 0 & -\frac{\pi\cdot\tau\cdot\beta\cdot\alpha}{\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2 - M_1\cdot M_3\cdot M_5\right)} \\ 0 & -\Gamma & 0 & 0 & 0 \\ 0 & 0 & -\Gamma & 0 & 0 \\ 0 & 0 & 0 & -\Gamma & 0 \\ 0 & 0 & 0 & 0 & -\Gamma \end{bmatrix}\right|$$

$$-\frac{\pi\cdot\tau\cdot\beta\cdot\Gamma^4\cdot M_5+\mu\cdot\tau\cdot\Gamma^5\cdot\alpha\cdot\rho_2-\mu\cdot\Gamma^5\cdot M_1\cdot M_3\cdot M_5}{\mu\cdot\tau\cdot\alpha\cdot\rho_2-\mu\cdot M_1\cdot M_3\cdot M_5}=0$$

$$-\Gamma^3\cdot\left[\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)\Gamma^2+\pi\cdot\tau\cdot\beta\cdot M_5\Gamma\right]=0$$

$$\left[\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)\Gamma^2+\pi\cdot\tau\cdot\beta\cdot M_5\Gamma\right]=0 \qquad (1.28)$$

Equation (1.28) is a quadratic equation of the form
$ax^2+bx+c=0$.
Where;

$$a:=\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)$$

$$b:=\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)$$

And $c=0$
We thus solve to get

$$\Gamma_1=\frac{-\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)+\sqrt{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)^2}}{2\cdot\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)}$$

And

$$\Gamma_2=\frac{-\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)-\sqrt{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)^2}}{2\cdot\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)}$$

$$\Gamma_2=\frac{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)+\sqrt{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)^2}}{2\cdot\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)}$$

$$R_0=\frac{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)+\sqrt{\left(\pi\cdot\tau\cdot\beta\cdot M_5\right)^2}}{2\cdot\mu\cdot\left(\tau\cdot\alpha\cdot\rho_2-M_1\cdot M_3\cdot M_5\right)}$$

Substituting the values of $M_1, M_3 and M_5$ we obtain the basic reproduction number R_0 for HBV as;

$$M_1:=\omega+\tau+\mu$$

$$M_3:=\rho_2+\rho_1-\theta$$

$$M_5:=\alpha+\mu+\delta+\lambda$$

$$R_0=\frac{[\pi\cdot\tau\cdot\beta\cdot(\alpha+\mu+\delta+\lambda)]+\sqrt{[\pi\cdot\tau\cdot\beta\cdot(\alpha+\mu+\delta+\lambda)]^2}}{2\cdot\mu\cdot\left[\tau\cdot\alpha\cdot\rho_2-(\omega+\tau+\mu)\cdot\left(\rho_2+\rho_1-\theta\right)\cdot(\alpha+\mu+\delta+\lambda)\right]} \qquad (1.29)$$

4.0 Results

4.1 Sensitivity indices of the Parameters of HBV

(1) The sensitivity index of *'π'* with respect to R_0 is given by

$$r_\pi^{R_0}=\frac{\partial R_0}{\partial\pi}\times\frac{\pi}{R_0}=+1.000$$

$$R_0=\frac{[\pi\cdot\tau\cdot\beta\cdot(\alpha+\mu+\delta+\lambda)]+\sqrt{[\pi\cdot\tau\cdot\beta\cdot(\alpha+\mu+\delta+\lambda)]^2}}{2\cdot\mu\cdot\left[\tau\cdot\alpha\cdot\rho_2-(\omega+\tau+\mu)\cdot\left(-\theta+\rho_2+\rho_1\right)\cdot(\alpha+\mu+\delta+\lambda)\right]}$$

$$R_0=\frac{[\Pi\cdot0.50\cdot0.37\cdot(0.01+0.021+0.068+0.015)]+\sqrt{[\Pi\cdot0.50\cdot0.37\cdot(0.01+0.021+0.068+0.015)]^2}}{2\cdot0.021\cdot[0.50\cdot0.01\cdot0.33-(0.02+0.50+0.021)\cdot(-10+0.33+0.33)\cdot(0.01+0.021+0.068+0.015)]}$$

$$\frac{d}{d\Pi}\frac{[\Pi\cdot 0.50\cdot 0.37\cdot(0.01+0.021+0.068+0.015)]+\sqrt{[\Pi\cdot 0.50\cdot 0.37\cdot(0.01+0.021+0.068+0.015)]^2}}{2\cdot 0.021\cdot[0.50\cdot 0.01\cdot 0.33-(0.02+0.50+0.021)\cdot(-10+0.33+0.33)\cdot(0.01+0.021+0.068+0.015)]}\cdot$$

$$\frac{\Pi}{\frac{[\Pi\cdot 0.50\cdot 0.37\cdot(0.01+0.021+0.068+0.015)]+\sqrt{[\Pi\cdot 0.50\cdot 0.37\cdot(0.01+0.021+0.068+0.015)]^2}}{2\cdot 0.021\cdot[0.50\cdot 0.01\cdot 0.33-(0.02+0.50+0.021)\cdot(-10+0.33+0.33)\cdot(0.01+0.021+0.068+0.015)]}}=1$$

$$=+1.000$$

Similarly, the value for other parameters of HBV are obtained in the same manner.

(2) The sensitivity index of *'β'* with respect to R_0 is given by

$$\mathrm{r}_{\beta}^{R_0}=\frac{\partial R_0}{\partial \beta}\times\frac{\beta}{R_0}=+1.000$$

Similarly, we can obtain the table below stating the sensitivity indexes of the various parameters of the model, thus;

Table 1: Numerical values of the Sensitivity indices of the Parameters of HBV

S/N	Parameters	Sensitivity index
1	π	$+1.000$
2	β	$+1.000$
3	τ	$+0.076$
4	ω	-0.037
5	α	-0.002606
6	λ	$+0.0003758$
7	ϕ	0.000
8	ρ_1	$+0.035$
9	ρ_2	$+0.032$
10	$\delta \Longrightarrow \Delta$	$+0.001704$
11	δ_1	0.000
12	μ	-1.038
13	$\varphi \Longrightarrow \Phi$	0.000
14	θ	-1.068
15	ψ	0.000

Table 2: Parameter values for HBV Infection

S/N	Parameter	Value	Reference
1	μ	0.021	[22, 26]
2	π	1000	Assumed
3	β	0.37	Assumed
4	τ	0.50	[27, 28]
5	θ	10	Assumed
6	ω	0.02	Assumed
7	α	0.01	Assumed
8	λ	0.015	[22]
9	ϕ	0.92	Assumed
10	ψ	0.015	[22]
11	$\varphi \Rightarrow \Phi$	0.08	[22]
12	ρ_1	0.33	[27, 28]
13	ρ_2	0.33	[27, 28]
14	δ	0.068	[22]
15	δ_1	0.068	[22]

5.0 Discussion of Results:

The results shows that some of the parameters have positive sign, some of the parameters have negative sign and some parameters also have zero. This implies that some of the parameters have positive effect on the basic reproduction number; some of the parameters have negative effect on the basic reproduction number while some have zero effect on the basic reproduction number of the model. The indices with positive signs show that the value of the basic reproduction number (R_0) increases when the values of the corresponding parameters are increased and decreases when the values of the corresponding parameters are decreased. Furthermore, those indices with negative signs indicates that the value of the basic reproduction number (R_0) increases when the value of the corresponding parameters are decreased and decreases when the value of the corresponding parameters are increased. The indices with zero shows that those parameters are not contributing to the cause of the infection.

From our results, let us take for instanceβ,which has the highest sensitivity index of +1. This means that R_0 is an increasing function of β. Thus, increasing (or decreasing) β by 20% will also increase (or decrease) R_0 by 20% . Similarly, the parameter θ which has the lowest sensitivity index of -1.068. This means that R_0 is a decreasing function of.θ Thus, increasing θ by 20% will also decrease R_0 by 20%. Conversely, decreasing θ by 20% will also increase R_0 by 20% .

Again , if the value of any parameter is negative, it implies that, that particular parameter can be used to control the disease dynamics, since increasing the value of that particular parameter will reduce the infection level of the disease. On the other hand, if the result is positive, it implies that , that parameter enhances the infectivity of the disease and so must be either avoided at all cost or must be targeted seriously in the control strategy to ensure that its value does not increase or conducive environment for its thriving is not allowed.

6.0 Conclusion

We computed the sensitivity indices of the basic reproduction number with respect to the model parameters. These sensitivity indices allowed us to determine the most influential (dominant) parameters in controlling the disease transmission and prevalence [22]. The sensitivity analysis result shows that; π(recruitment) and β(contact rate for HBV infectious individuals with the susceptible individuals) with sensitivity index of $+1.00$ each are the most sensitive parameters that affect the transmission dynamics of HBV infection in the population since these parameters enhances the infectivity of the disease, and so must be targeted seriously in the control strategy to ensure that its value does not increase.

7.0 References

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