Mathematical Analysis of the Control of Hepatitis B Virus in a Population with Vital Dynamics.

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ABSTRACT

In this paper, we developed and analysed a new mathematical model for the dynamics of hepatitis B virus (HBV) in a population with vital dynamics, incorporating vertical transmission, sexual maturity, the effect of public enlightenment campaign with respect to sexual behaviour, and vaccination as control measures. We obtained the effective basic reproduction number R_c which can be used to control the transmission of the disease and hence, established the conditions for local and global stability of the disease free equilibrium. Bifurcation analysis was carried out using centre manifold theory which reveals a subcritical (backward) bifurcation for the model. Numerical simulations validated the analytical results and further reveals that HBV vaccination for sexually active individuals as the only control strategy can control (eliminate) the disease at even a low level of vaccination compliance.

(Keywords: HBV, stability, effective basic reproduction number)

INTRODUCTION

Hepatitis (plural Hepatitides) is a general term that means injury to the liver characterized by the presence of inflammatory cells in the tissue of the organ (liver). Hepatitis B is a disease caused by hepatitis B virus (HBV). This disease reduces the liver's ability to perform life-preserving functions, including filtering harmful infectious agents from the blood, storing blood sugar and converting it to usable energy forms, and producing many proteins necessary for life.

Hepatitis B is fifty to one hundred times more infectious than HIV (WHO, 2009 and Adeoye, 2010). It has caused epidemics in part of Asia and Africa, and it is endemic in China (Williams, 2006). About a third of the world's population, more than two billion peoples have been infected with hepatitis B virus (Long et al., 2008). This includes 350 million chronic carriers of the virus (Dahari et al., 2009).

Transmission of hepatitis B virus results from exposure to infectious blood or body fluids containing blood. Possible forms of transmissions include (but are not limited to) unprotected sexual contact, blood transfusions, re-use of contaminated needles and syringes, and vertical transmission from mother to child during child birth. Between 90 to 95% of all babies born to infected mothers get the disease during birth.

Infection with the HBV has been a major public health problem. This has two phases: Acute and Chronic. The Acute phase causes liver inflammation, vomiting, and jaundice in which the individual is infectious. Chronic hepatitis B is an infection with hepatitis B virus that last longer than six months. Once the infection becomes chronic, it may never go away completely, and may eventually cause liver cirrhosis and hepatocellular carcinoma (HCC) (Long et al., 2008 and Hoofnagle et al., 2007). HBV causes approximately 600,000 deaths each year world-wide. Moreover, 10% of people (i.e. approximately four million people world-wide) infected with HIV are co-infected with HBV (Dahari et al., 2009).

In order to find an efficient way to control (prevent and treat) an infection, it is of great importance to establish its transmission dynamics. One main goal of mathematical epidemiology is to understand how to control and eradicate diseases (Ma and Ma, 2006). Mathematical models are used extensively in the study of ecological and epidemiological phenomena (Kaplan and

Brandeau, 1994). They are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological and environmental factors on the spread of diseases. This is so because they can help in figuring out decisions that are of significance importance on the outcomes and provide comprehensive examinations that enter into decisions in a way that human reasoning and debate cannot.

During the last two and a half decades, Pasquini et al. (1987), Williams et al. (1996), Zhao et al. (2000), Medley et al. (2001), Sutton et al. (2006), Thorley et al. (2008), Zou et al. (2010) have designed mathematical models to evaluate the effect of public health programs and provided long-term predictions regarding HBV prevalence and control in various region. Considering the work of all the authors mentioned above, we developed a new mathematical model improving on their works by incorporating the following factors which are very important in the transmission and control of hepatitis B virus especially in developing countries where the disease is endemic.

i) Vital dynamics (number of birth not equal to number of death);
ii) Vertical transmission;
iii) Public enlightenment;
iv) Condom usage;
v) Standard incidence function;
vi) Disease induced death due to both acute and chronic infection;
vii) Waning of immunization and
viii) Sexual maturity.

In this paper we formulate the model, analyze the model by obtaining the effective basic reproduction number, R_c and establishing the conditions for local and global stability of the disease free equilibrium, and carry out Bifurcation analysis using centre manifold theory. We follow these sections with a discussion of the results.

MODEL FORMULATION

We formulate a model for the spread and control of HBV in the human population with the total population size at time, t given by $N(t)$. The total population is compartmentalized into 8 epidemiological classes shown below. Our model incorporated immunization given to only susceptible individuals. Disease induced death occurs in all the infected classes at different rates, while natural death occurs equally in all classes. Our model has the following variables and parameters.

$S_U(t)$ Number of susceptible individuals under 15 years of age at time t

$S_F(t)$ Number of susceptible individuals at or above 15 years of age at time t

$V(t)$ Number of vaccinated individuals at time t

$A_U(t)$ Number of acutely infected individuals under 15 years of age at time t

$A_F(t)$ Number of acutely infected individuals at or above 15 years of age at time t

$C_U(t)$ Number of chronically infected individuals under 15 years of age at time t

$C_F(t)$ Number of chronically infected individuals at or above 15 years of age at time t

$R(t)$ Number of removed individuals due to recovery from infection at time t

b Per capital birth rate of humans

μ Per capital natural death rate

δ_A HBV-induced death rate by A_U and A_F

δ_C HBV-induced death rate by C_F

c Average number of sexual partner

p HBV-Sexual transmission risk rate and therefore pc is the effective sexual contact rate

η Modification parameter associated with reduced sexual transmission rate by chronic individuals

ε_c Condom efficacy

τ_c Condom compliance

ε_ρ Vaccine efficacy

τ_b Vaccine compliance at birth and therefore $\rho_b = \varepsilon_\rho \tau_b$ is the effective immunization rate for individuals at birth.

τ_U Vaccine compliance not at birth by S_U and therefore $\rho_U = \varepsilon_\rho \tau_U$ is the effective immunization rate for individuals under-fifteen years of age but not at birth.

τ_F Vaccine compliance by S_F and therefore $\rho_F = \varepsilon_\rho \tau_F$ is the effective immunization rate for individuals at or above fifteen years of age.

ω Loss (waning) of vaccination immunity

θ Proportion of HBV- positive birth

ϕ Modification parameter associated with reduced HBV – positive birth by C_F

σ_S Rate of moving from S_U to S_F

σ_A Rate of moving from acutely infected classes to chronically infected / removed classes

σ_C Rate of moving from C_U to C_F

φ_U Proportion of A_U which progresses to C_U, while $(1-\varphi_U)$ become removed and therefore $\gamma_{AU} = \sigma_A(1-\varphi_U)$ is the recovery rate from A_U to R

φ_F Proportion of A_F which progresses to C_F, while $(1-\varphi_F)$ become removed and therefore $\gamma_{AF} = \sigma_A(1-\varphi_F)$ is the recovery rate from A_F to R

γ_{CF} Rate of recovery from C_F to R

Figure 1 below is a schematic representation of the model and the corresponding mathematical equations of the schematic diagram can be described by a system of ordinary differential equations given below.

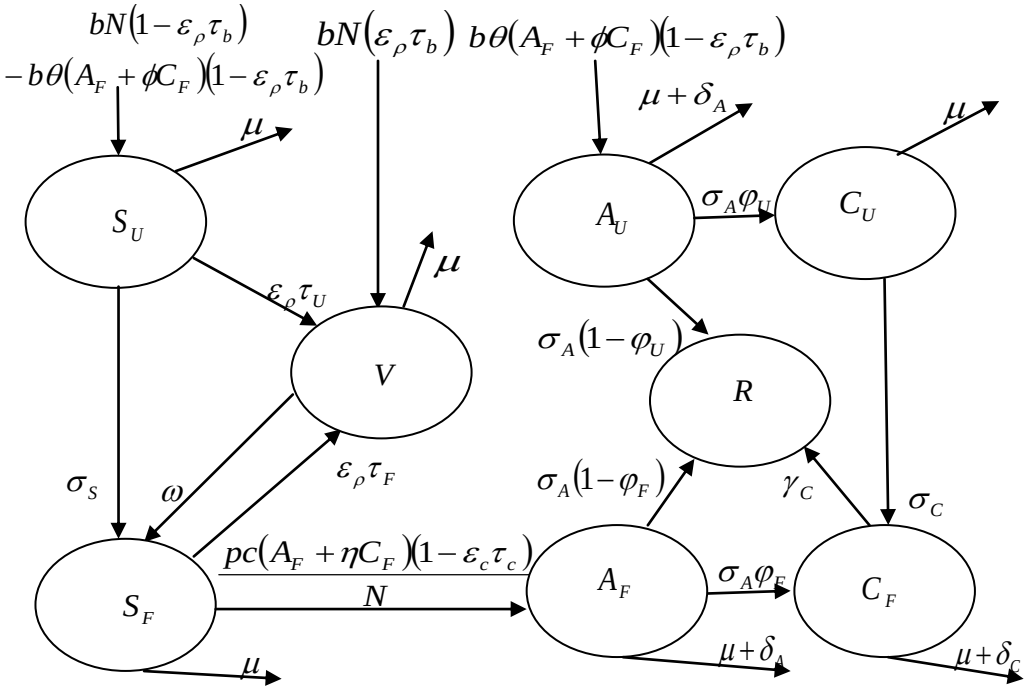

Figure 1: Schematic Diagram of HBV Transmission and Control Model.

$$
\begin{aligned}
\frac{dS_U}{dt} &= bN(1-\varepsilon_\rho\tau_b) - b\theta(A_F+\phi C_F)(1-\varepsilon_\rho\tau_b) - (\sigma_S+\varepsilon_\rho\tau_U+\mu)S_U \\
\frac{dS_F}{dt} &= \sigma_S S_U + \omega V - \frac{pc(A_F+\eta C_F)(1-\varepsilon_c\tau_c)}{N}S_F - (\varepsilon_\rho\zeta_F+\mu)S_F \\
\frac{dV}{dt} &= bN(\varepsilon_\rho\tau_b) + (\varepsilon_\rho\tau_U)S_U + (\varepsilon_\rho\tau_F)S_F - (\omega+\mu)V \\
\frac{dA_U}{dt} &= b\theta(A_F+\phi C_F)(1-\varepsilon_\rho\tau_b) - (\sigma_A+\mu+\delta_A)A_U \\
\frac{dA_F}{dt} &= \frac{pc(A_F+\eta C_F)(1-\varepsilon_c\tau_c)}{N}S_F - (\sigma_A+\mu+\delta_A)A_F \\
\frac{dC_U}{dt} &= \sigma_A\varphi_U A_U - (\sigma_C+\mu)C_U \\
\frac{dC_F}{dt} &= \sigma_A\varphi_F A_F + \sigma_C C_U - (\gamma_{CF}+\mu+\delta_C)C_F \\
\frac{dR}{dt} &= \sigma_A(1-\varphi_U)A_U + \sigma_A(1-\varphi_F)A_F + \gamma_{CF}C_F - \mu R
\end{aligned}
\qquad \textbf{(1)}
$$

where,

$$
\begin{aligned}
N(t) = S_U(t) + S_F(t) + V(t) + A_U(t) \\
+ A_F(t) + C_U(t) + C_F(t) + R(t)
\end{aligned}
\qquad \textbf{(2)}
$$

So that,

$$
\frac{dN}{dt} = (b-\mu)N - \delta_A(A_U+A_F) - \delta_C C_F \qquad \textbf{(3)}
$$

The following assumptions are taken into account in the construction of the model.

1. There is homogeneous mixing of the population, where all people are equally likely to be infected by the infectious individuals in case of contact;

2. Public enlightenment (PE) is given to all classes and the higher the PE on HBV immunization and condom usage, the higher the compliance respectively;

3. HBV vaccination immunity wanes after 25 years as it since it has not yet been established to be life-long.

Consider Equations (1) for the normalized quantities. Since, it is better and easier (convenient) to analyze our model in terms of proportions of quantities instead of actual populations as described in Busenberg (1990), Akinwande (1996), Li et al. (1999), Hethcote (2000), Tumwiine et al. (2007), Capasso (2008), and Benyah (2008). This can be done by scaling the population of each class by the total populations N. We let:

$$
s_U = \frac{S_U}{N}, s_F = \frac{S_F}{N}, v = \frac{V}{N}, a_U = \frac{A_U}{N},
$$

$$
a_F = \frac{A_F}{N}, c_U = \frac{C_U}{N}, c_F = \frac{C_F}{N} \text{ and } r = \frac{R}{N}
$$

denote the fractions of the classes $S_U, S_F, V, A_U, A_F, C_U, C_F$ and R in the population respectively. This is done by differentiating the fractions (using quotient rule) with respect to time, *t*. Then simplifying, we have from (1) and (3) we have Equation 4.

$$\frac{ds_U}{dt} = b(1-\rho_b) - (b_A a_F + b_C c_F) - K_1 s_U + (\delta_A(a_U + a_F) + \delta_C c_F)s_U$$

$$\frac{ds_A}{dt} = \sigma_S s_U + \omega v - (\alpha_A a_F + \alpha_C c_F)s_F - K_2 s_F + (\delta_A(a_U + a_F) + \delta_C c_F)s_F$$

$$\frac{dv}{dt} = b\rho_b + \rho_U s_U + \rho_F s_F - K_3 v + (\delta_A(a_U + a_F) + \delta_C c_F)v$$

$$\frac{da_U}{dt} = (b_A a_F + b_C c_F) - K_4 a_U + (\delta_A(a_U + a_F) + \delta_C c_F)a_U$$

$$\frac{da_F}{dt} = (\alpha_A a_F + \alpha_C c_F)s_F - K_4 a_F + (\delta_A(a_U + a_F) + \delta_C c_F)a_F$$

$$\frac{dc_U}{dt} = \sigma_A \varphi_U a_U - K_5 c_U + (\delta_A(a_U + a_F) + \delta_C c_F)c_U$$

$$\frac{dc_F}{dt} = \sigma_A \varphi_F a_F + \sigma_C c_U - K_6 c_F + (\delta_A(a_U + a_F) + \delta_C c_F)c_F \quad \textbf{(4)}$$

$$\frac{dr}{dt} = (1-\varphi_U)\sigma_A a_U + (1-\varphi_A)\sigma_A a_F + \gamma_C c_F - br + (\delta_A(a_U + a_F) + \delta_C c_F)r$$

in the biological - feasible region:

$$\Omega = \left\{ \begin{array}{l} (s_U, s_F, v, a_U, a_F, c_U, c_F, r) \in \mathrm{R}_+^8 : \\ s_U + s_F + v + a_U + a_F + c_U \\ \qquad + c_F + r = 1 \end{array} \right\} \quad \textbf{(5)}$$

Where,

$$\rho_b = \varepsilon_\rho \tau_b,\ \rho_U = \varepsilon_\rho \tau_U,\ \rho_F = \varepsilon_\rho \tau_F$$
$$b_A = b\theta(1-\varepsilon_\rho \tau_b), b_C = b\theta\phi(1-\varepsilon_\rho \tau_b)$$
$$\alpha_A = pc(1-\varepsilon_c \tau_c),\ \alpha_C = pc\eta(1-\varepsilon_c \tau_c)$$
$$\gamma_{AU} = \sigma_A(1-\varphi_U),\ \gamma_{AF} = \sigma_A(1-\varphi_F) \quad \textbf{(6)}$$
$$K_1 = (\sigma_S + \rho_U + b),\ K_2 = (\rho_F + b)$$
$$K_3 = (\omega + b),\ K_4 = (\sigma_A + b + \delta_A)$$
$$K_5 = (\sigma_C + b),\ K_6 = (\gamma_C + b + \delta_C)$$

which can be shown to be positively invariant with respect to the system (4). We note that the total population size $N(t)$ does not appear in (4); this is as a direct result of the homogeneity of Equations (1).

MODEL ANALYSIS

We now determine the existence of equilibria points; computing the effective basic reproduction number; and establishing the conditions for stability of the equilibria points.

Existence of Disease Free Equilibrium State, E_f

At the disease free equilibrium state we have absence of infection. Thus, all the infected classes will be zero and the entire population will comprise of susceptible and vaccinated individuals. At equilibrium state the rate of change of each variable is equal to zero, i.e.,

$$\frac{dN}{dt} = \frac{ds_U}{dt} = \frac{ds_F}{dt} = \frac{dv}{dt} = \frac{da_U}{dt} = \frac{da_F}{dt} = \frac{dc_U}{dt} = \frac{dc_F}{dt} = 0$$

let,

$$(s_U, s_F, v, a_U, a_F, c_U, c_F) = (s_U^*, s_F^*, v^*, a_U^*, a_F^*, c_U^*, c_F^*)$$

at equilibrium state. Thus, substituting into (4) with $a_U^* = a_F^* = c_U^* = c_F^* = 0$, we obtained the disease – free equilibrium state given by:

$$(s_U^*, s_F^*, v^*, a_U^*, a_F^*, c_U^*, c_F^*, r^*) = \left(\frac{b(1-\rho_b)}{K_1}, \frac{b\{(K_3\sigma_S + \omega\rho_U)(1-\rho_b) + K_1\omega\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, \frac{b\{(1-\rho_b)(K_2\rho_U + \sigma_S\rho_F) + K_2K_1\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, 0,0,0,0,0 \right) \quad \textbf{(7)}$$

Effective Basic Reproduction Number, R_c

Consideration of stability of a disease-free equilibrium gives certain conditions under which disease will die out or stay in the population called the Basic reproduction number, R_0. Using the approach of Diekmann and Heesterbeek (2000) we obtained the effective basic

reproduction number, R_c of the system (4) which is the spectral radius (ρ) of the next generation matrix, K, i.e.,

$R_c = \rho K$, where $K = FV^{-1}$

Now,

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & \alpha_A s_F^{*} & 0 & \alpha_C s_F^{*} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and}$$

$$V = \begin{pmatrix} K_4 & -b_A & 0 & -b_C \\ 0 & K_4 & 0 & 0 \\ -\sigma_A\varphi_U & 0 & K_5 & 0 \\ 0 & -\sigma_A\varphi_F & -\sigma_C & K_6 \end{pmatrix}$$

Then,

$$R_C = \frac{\alpha_A s_F^{*}}{K_4}\left(1 + \frac{\eta\sigma_A\left(K_4K_5\varphi_F + \sigma_C\varphi_U b_A\right)}{\left(K_4K_5K_6 - \sigma_C\sigma_A\varphi_U b_C\right)}\right) \quad \textbf{(8)}$$

i.e.,

$$R_C = \frac{\left\{\begin{array}{r}\left((\omega+b)\sigma_S + \omega\rho_U\right)(1-\rho_b) \\ +\left(\sigma_S + \rho_U + b\right)\omega\rho_b\end{array}\right\}}{\left(\sigma_S + \rho_U + b\right)\left(\rho_F + b + \omega\right)} \times \frac{pc(1-\varepsilon_c\tau_c)}{\left(\sigma_A + b + \delta_A\right)} \times \left(1 + \frac{\eta\sigma_A\left(\begin{pmatrix}\sigma_A + b \\ +\delta_A\end{pmatrix}(\sigma_C + b)\varphi_F + \sigma_C\varphi_U b_A\right)}{\left(\begin{pmatrix}\sigma_A + b \\ +\delta_A\end{pmatrix}(\sigma_C + b)\begin{pmatrix}\gamma_{Cf} + b \\ +\delta_C\end{pmatrix} - \sigma_C\sigma_A\varphi_U b_C\right)}\right) \quad \textbf{(9)}$$

And thus,

$$R_0 = \frac{\sigma_S}{(\sigma_S + b)} \times \frac{pc(1-\varepsilon_c\tau_c)}{(\sigma_A + b + \delta_A)} \times \left(1 + \frac{\eta\sigma_A\left(\begin{pmatrix}\sigma_A + b \\ +\delta_A\end{pmatrix}(\sigma_C + b)\varphi_F + \sigma_C\varphi_U b_A\right)}{\left(\begin{pmatrix}\sigma_A + b \\ +\delta_A\end{pmatrix}(\sigma_C + b)(\gamma_{Cf} + b + \delta_C) - \sigma_C\sigma_A\varphi_U b_C\right)}\right) \quad \textbf{(10)}$$

Local Stability of Disease Free Equilibrium, E_f

We used the Jacobian stability approach to prove the stability of the disease free equilibrium state. Now, we observed that the variable *r* does not appear in the first seven equations of (4). Using the relation:

$$r = 1 - s_U - s_F - a_U - a_F - c_U - c_F > 0 \quad \textbf{(11)}$$

allows us as explained in Hecthote (2000), Benyah (2008) to attack (3.4) by studying the subsystem:

$$\begin{aligned}
\frac{ds_U}{dt} &= b(1-\rho_b) - \left(b_A a_F + b_C c_F\right) \\
&\quad - K_1 s_U + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)s_U \\
\frac{ds_A}{dt} &= \sigma_S s_U + \omega v - \left(\alpha_A a_F + \alpha_C c_F\right)s_F \\
&\quad - K_2 s_F + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)s_F \\
\frac{dv}{dt} &= b\rho_b + \rho_U s_U + \rho_F s_F \\
&\quad - K_3 v + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)v \\
\frac{da_U}{dt} &= \left(b_A a_F + b_C c_F\right) \\
&\quad - K_4 a_U + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)a_U \\
\frac{da_F}{dt} &= \left(\alpha_A a_F + \alpha_C c_F\right)s_F \\
&\quad - K_4 a_F + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)a_F \\
\frac{dc_U}{dt} &= \sigma_A\varphi_U a_U \\
&\quad - K_5 c_U + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)c_U \\
\frac{dc_F}{dt} &= \sigma_A\varphi_F a_F + \sigma_C c_U \\
&\quad - K_6 c_F + \left(\delta_A\left(a_U + a_F\right) + \delta_C c_F\right)c_F
\end{aligned} \quad \textbf{(12)}$$

linearization of the Equations in (12) at E_f gives the Jacobian matrix:

$$J(E_f)=\begin{pmatrix} -K_1 & 0 & 0 & \delta_A s_U^* & -b_A+\delta_A s_U^* & 0 & -b_C+\delta_C s_U^* \\ \sigma_S & -K_2 & \omega & \delta_A s_F^* & -(\alpha_A-\delta_A)s_F^* & 0 & -(\alpha_C-\delta_C)s_F^* \\ \rho_U & \rho_F & -K_3 & \delta_A v^* & \delta_A v^* & 0 & \delta_C v^* \\ 0 & 0 & 0 & -K_4 & b_A & 0 & b_C \\ 0 & 0 & 0 & 0 & -K_{4n} & 0 & \alpha_C s_F^* \\ 0 & 0 & 0 & \sigma_A\varphi_U & 0 & -K_5 & 0 \\ 0 & 0 & 0 & 0 & \sigma_A\varphi_F & \sigma_C & -K_6 \end{pmatrix}$$

(13)

where,

$$K_{4n}=\left(K_4-\alpha_A s_F^*\right)>0 \qquad \textbf{(14)}$$

Using elementary row-transformation, we have:

$$=\begin{pmatrix} -K_1 & 0 & 0 & \delta_A s_U^* & -b_A+\delta_A s_U^* & 0 & -b_C+\delta_C s_U^* \\ 0 & -K_2 & \omega & M_1 & -M_2 & 0 & -M_3 \\ 0 & 0 & -K_3+\frac{\rho_F\omega}{K_2} & M_4 & M_5 & 0 & M_6 \\ 0 & 0 & 0 & -K_4 & b_A & 0 & b_C \\ 0 & 0 & 0 & 0 & -K_{4n} & 0 & \alpha_C s_F^* \\ 0 & 0 & 0 & 0 & 0 & -K_5 & M_7 \\ 0 & 0 & 0 & 0 & 0 & 0 & M_8 \end{pmatrix}$$

(15)

where,

$$M_1=\delta_A s_F^*+\frac{\sigma_S\delta_A s_U^*}{K_1}$$

$$M_2=\left((\alpha_A-\delta_A)s_F^*+\frac{\sigma_S\left(b_A-\delta_A s_U^*\right)}{K_1}\right)$$

$$M_3=\left((\alpha_C-\delta_C)s_F^*+\frac{\sigma_S\left(b_C-\delta_C s_U^*\right)}{K_1}\right)^*-\frac{\rho_U\left(b_C-\delta_C s_U^*\right)}{K_1}$$

$$M_4=\delta_A v^*+\frac{\rho_U\delta_A s_U^*}{K_1}$$

$$M_5=\delta_A v^*-\frac{\rho_U\left(b_A-\delta_A s_U^*\right)}{K_1}$$

$$M_6=\delta_C v^*-\frac{\rho_U\left(b_C-\delta_C s_U^*\right)}{K_1}$$

$$M_7=\frac{\sigma_A\varphi_U b_C}{K_4}+\frac{\sigma_A\varphi_U b_A\alpha_C s_F^*}{K_4K_4n}$$

$$M_8=-K_6+\frac{\sigma_A\varphi_F\alpha_C s_F^*}{K_4n}+\frac{\sigma_C}{K_5}\left(\frac{\sigma_A\varphi_U b_C}{K_4}+\frac{\sigma_A\varphi_U b_A\alpha_C s_F^*}{K_4K_4n}\right)$$

Thus, the eigenvalues are:

$$\lambda_1=-(\sigma_S+\rho_U+b)<0$$
$$\lambda_2=-(\rho_F+b)<0$$
$$\lambda_3=\frac{-b(\omega+\rho_F+b)}{(\rho_F+b)}<0,$$
$$\lambda_4=-(\sigma_A+b+\delta_A)<0$$
$$\lambda_5=-\left(K_4-\alpha_A s_F^*\right)<0$$
$$\lambda_6=-(\gamma_C+b+\delta_C)<0$$

and

$$\lambda_7=-K_6+\frac{\sigma_A\varphi_F\alpha_C s_F^*}{K_{4n}}+\frac{\sigma_C}{K_5}\left(\frac{\sigma_A\varphi_U b_C}{K_4}+\frac{\sigma_A\varphi_U b_A\alpha_C s_F^*}{K_4K_{4n}}\right)$$

now, for λ_7 to be negative, we should have,

$$-K_6+\frac{\sigma_A\varphi_F\alpha_C s_F^*}{K_{4n}}+\frac{\sigma_C}{K_5}\left(\frac{\sigma_A\varphi_U b_C}{K_4}+\frac{\sigma_A\varphi_U b_A\alpha_C s_F^*}{K_4K_{4n}}\right)<0$$

Simplifying, we have,

$$\frac{\alpha_A s_F^*}{K_4}\left(1+\frac{\eta\sigma_A(\varphi_F K_4K_5+\sigma_C\varphi_U b_A)}{K_4(K_6K_5K_4-\sigma_C\sigma_A\varphi_U b_C)}\right)<1$$

i.e., $R_c<1$.

Obviously, if $R_c<1$, λ_7 is negative, implying all the eigenvalues have negative real parts, we thus, established the following result.

Theorem 1: The disease- free equilibrium E_f of (3.4) is locally asymptotically stable (LAS) if $R_C<1$.

Global Stability of Disease Free Equilibrium, E_f

The epidemiological implication of the theorem is that HBV can be eliminated (control) from the population when $R_C < 1$, if the initial size of the sub-populations of the model are in the basin of attraction of the DFE.

In order to ensure that HBV is independent of the initial size of the sub-populations of the model (4), it is necessary to show that the DFE is globally-asymptotically stable (GAS). One common approach in studying the global asymptotic stability of the DFE is to construct an appropriate Lyapunov function (Li et al., 1999, Fall et al., 2007, Huo et al., 2010, Garba and Gumel, 2010). However, we applied the result introduced by Castillo-Chavez et al. (2002).

Theorem 2: The disease- free equilibrium E_f of (4) is globally asymptotically stable (GAS) in Ω if $R_C < 1$.

Proof: To establish the global stability of the disease free equilibrium, the two conditions (H1) and (H2) as in Castillo-Chavez et al. (2002) must be satisfied for $R_C < 1$. We rewrite the model (4) in the form:

$$\begin{aligned} \frac{dX_1}{dt} &= F(X_1, X_2) \\ \frac{dX_2}{dt} &= G(X_1, X_2);\ G(X_1, 0) = 0 \end{aligned} \qquad \textbf{(16)}$$

where,

$$X_1 = \left(s_U^*, s_F^*, v^*, r^*\right), X_2 = \left(a_U^*, a_F^*, c_U^*, c_F^*\right)$$

with the components of $X_1 \in R^4$ denoting the uninfected population and the components of $X_2 \in R^4$ denoting the infected population.

The disease-free equilibrium is now denoted as:

$$E_f = \left(X_1^*, 0\right)$$

$$X_1^* = \left(\frac{b(1-\rho_b)}{K_1}, \frac{b\{(K_3\sigma_S + \omega\rho_U)(1-\rho_b) + K_1\omega\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, \frac{b\{(1-\rho_b)(K_2\rho_U + \sigma_S\rho_F) + K_2K_1\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, 0 \right)$$

Now, for the first condition, that is globally asymptotically stability of X_1^*, we have,

$$\frac{dX_1}{dt} = F(X_1, 0) = \begin{bmatrix} b(1-\rho_b) - K_1 s_U^* \\ \sigma_S s_U^* + \omega v^* - K_2 s_F^* \\ b\rho_U + \rho_U s_U^* + \rho_F s_F^* - K_3 v^* \\ -br^* \end{bmatrix}$$

a linear differential equation.

Solving, we have:

$$s_U^*(t) = \frac{b(1-\rho_b)}{K_1} - \frac{b(1-\rho_b)}{K_1} e^{-K_1 t} + s_U^*(0) e^{-K_1 t}$$

$$s_F^*(t) = \frac{\sigma_S s_U^* + \omega v^*}{K_2} - \frac{\sigma_S s_U^* + \omega v^*}{K_2} e^{-K_2 t} + s_F^*(0) e^{-K_2 t}$$

$$v^*(t) = \frac{\left(b\rho_U + \rho_U s_U^* + \rho_F s_F^*\right)}{K_3} - \frac{\left(b\rho_U + \rho_U s_U^* + \rho_F s_F^*\right)}{K_3} e^{-K_2 t} + v^*(0) e^{-K_2 t}$$

and

$$r^*(t) = r^*(0) e^{-bt}$$

Now, clearly we have:

$$s_U^*(t) + s_F^*(t) + v^*(t) + r^*(t) \to 1 \text{ as } t \to \infty,$$

regardless of the value of

$$s_U^*(0), s_F^*(0), v^*(0) \text{ and } r^*(0).$$

Thus $X_1^* = \begin{pmatrix} \frac{b(1-\rho_b)}{K_1}, \frac{b\{(K_3\sigma_S + \omega\rho_U)(1-\rho_b) + K_1\omega\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, \\ \frac{b\{(1-\rho_b)(K_2\rho_U + \sigma_S\rho_F) + K_2K_1\rho_b\}}{K_1(K_2K_3 - \omega\rho_F)}, 0 \end{pmatrix}$

is globally asymptotically stable.

Next, for the second condition, that is $\hat{G}(X_1, X_2) = AX_2 - G(X_1, X_2)$, we have:

$$A = \begin{bmatrix} -K_4 & b_A & 0 & b_C \\ 0 & -K_{4n} & 0 & \alpha_C s_F^* \\ \sigma_A\varphi_U & 0 & -K_5 & 0 \\ 0 & \sigma_A\varphi_F & \sigma_C & -K_6 \end{bmatrix}$$

This is clearly an M-matrix (the off-diagonal elements of A are non-negative).

$$G(X_1, X_2) = \begin{bmatrix} \left(b_A a_F^* + b_C c_F^*\right) - K_4 a_U^* \\ \quad + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_U^* \\ \left(\alpha_A a_F^* + \alpha_C c_F^*\right) s_F^* - K_4 a_F^* \\ \quad + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_F^* \\ \varphi_U\sigma_A a_U^* - K_5 c_U^* \\ \quad + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_U^* \\ \varphi_F\sigma_A a_F^* + \sigma_C c_U^* - K_6 c_F^* \\ \quad + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_F^* \end{bmatrix}$$

then,

$$\hat{G}(X_1, X_2) = AX_2 - G(X_1, X_2) = \begin{bmatrix} \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_U^* \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_F^* \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_U^* \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_F^* \end{bmatrix}$$

i.e.,

$$\hat{G}(X_1, X_2) = \begin{bmatrix} \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_U^*, \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) a_F^* \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_U^*, \\ \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) c_F^* \end{bmatrix}^T$$

Since all parameters are assumed non-negative, we have,

$$\left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right) \geq 0$$

It is thus obvious that $\hat{G}(X_1, X_2) \geq 0$. Hence, the proof is complete.

Existence of Endemic Equilibrium State, E^*

The endemic equilibrium state is the state in which the disease is persistence. That is the coordinates should satisfy the conditions:

$$E^* = \left(s_U^*, s_F^*, v^*, a_U^*, a_F^*, c_U^*, c_F^*\right): \\ s_U^* > 0, s_F^* > 0, v^* > 0, a_U^* > 0, \\ a_F^* > 0, c_U^* > 0, c_F^* > 0$$

As described in Akinwande (1996) and Hethcote (2000), it is too cumbersome to explicitly find the coordinates points of the endemic state in models with vital dynamic (births not equal to deaths), standard incidence and disease induced death, but at least we can prove its existence.

Now, global stability of the disease free equilibrium (Theorem 2), E_f in Ω precludes the existence of equilibrium other than E_f, since the study of endemic equilibrium is restricted to the case $R_0 > 1$. Adding the equations of the system (3.4), at equilibrium state, gives:

$$\begin{aligned} &b(1-\rho_b) - \left(b_A a_F^* + b_C c_F^*\right) - (\sigma_S + b)s_U^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)s_U^* \\ &+ \sigma_S s_U^* + \omega v^* - \left(\alpha_A a_F^* + \alpha_C c_F^*\right)s_F^* - bs_F^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)s_F^* \\ &+ b\rho_b + \rho_U s_U^* + \rho_F s_F^* - (\omega + b)v^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)v^* \\ &+ \left(b_A a_F^* + b_C c_F^*\right) - (\sigma_A + b + \delta_A)a_U^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)a_U^* \\ &+ \left(\alpha_A a_F^* + \alpha_C c_F^*\right)s_F^* - (\sigma_A + b + \delta_A)a_F^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)a_F^* \\ &+ \varphi_U\sigma_A a_U^* - (\sigma_C + b)c_U^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)c_U^* \\ &+ \varphi_F\sigma_A a_F^* + \sigma_C c_U^* - (\gamma_C + b + \delta_C)c_F^* + \left(\delta_A\left(a_U^* + a_F^*\right) + \delta_C c_F^*\right)c_F^* = 0 \end{aligned}$$

Simplifying, we have:

$$\begin{aligned} &\left(b - \left(\delta_A a_U^* + \delta_A a_F^* + \delta_C c_F^*\right)\right)\times \\ &\left(1 - s_U^* - s_F^* - v^* - a_U^* - a_F^* - c_U^* - c_F^*\right) \\ &= \sigma_A(1-\varphi_U)a_U^* + \sigma_A(1-\varphi_F)a_F^* + \gamma_C c_F^* \end{aligned} \quad \textbf{(17)}$$

since all parameters are non-negative, we have R.H.S > 0 and from (11),

$$\left(1-s_U^{\,*}-s_F^{\,*}-v^*-a_U^{\,*}-a_F^{\,*}-c_U^{\,*}-c_F^{\,*}\right)>0$$

then,

$$\left(\delta_A a_U^{\,*}+\delta_A a_F^{\,*}+\delta_C c_F^{\,*}\right)<b$$

$$\Rightarrow a_U^{\,*}<\frac{b}{\delta_A}, a_F^{\,*}<\frac{b}{\delta_A}, c_F^{\,*}<\frac{b}{\delta_C}$$

i.e.,

$$a_U^{\,*}>0, a_U^{\,*}<1, a_U^{\,*}<\frac{b}{\delta_A}$$

$$a_F^{\,*}>0, a_F^{\,*}<1, a_F^{\,*}<\frac{b}{\delta_A} \text{ and}$$

$$c_F^{\,*}>0, c_F^{\,*}<1, c_F^{\,*}<\frac{b}{\delta_C}$$

which gives the following range of :

$$0<a_U^{\,*}<\min\left\{1,\frac{b}{\delta_A}\right\}$$

$$0<a_F^{\,*}<\min\left\{1,\frac{b}{\delta_A}\right\}, \text{ and}$$

$$0<c_F^{\,*}<\min\left\{1,\frac{b}{\delta_C}\right\}$$

Thus, an endemic equilibrium point exists, where $a_U^{\,*}, a_F^{\,*}$, and $c_F^{\,*}$, lies in the interval,

$$\left(0,\min\left\{1,\frac{b}{\delta_A}\right\}\right),\left(0,\min\left\{1,\frac{b}{\delta_A}\right\}\right) \text{ and } \left(0,\min\left\{1,\frac{b}{\delta_C}\right\}\right)$$

Remark

The relation $b>\delta_A$ and $b>\delta_C$ is of great importance and plays a great role when HBV persists. It shows that mortality rate due to HBV infection should be less than that at which the susceptible population is refilled due to birth. Thus we remark that $R_C>1$ implies $b>\delta_A$ and $b>\delta_C$.

Bifurcation Analysis

We used the centre manifold theory as described in Castillo-Chavez and Song (2004) for bifurcation analysis. In order to apply the theorem, we make the following change of variables. Let

$$s_U=x_1, s_F=x_2, v=x_3, a_U=x_4$$
$$a_F=x_5, c_U=x_6, c_F=x_7$$

further by using the vector notation

$$X=\left(x_1,x_2,x_3,x_4,x_5,x_6,x_7\right)^T$$

the model in (4) can be written in the form,

$$\frac{dX}{dt}=F=\left(f_1,f_2,f_3,f_4,f_5,f_6,f_7\right)^T$$

such that:

$$\begin{aligned}
\frac{dx_1}{dt}&=f_1=b(1-\rho_b)-\left(b_A x_5+b_C x_7\right)-k_1x_1\\
&\quad+\omega x_3+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_1\\
\frac{dx_2}{dt}&=f_2=\sigma_S x_1-\left(\alpha_A x_5+\alpha_C x_7\right)x_2\\
&\quad-k_2x_2+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_2\\
\frac{dx_3}{dt}&=f_3=b\rho_b+\rho_U x_1+\rho_F x_2-K_3x_3\\
&\quad+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_3\\
\frac{dx_4}{dt}&=f_4=\left(b_A x_5+b_C x_7\right)-k_4x_4\\
&\quad+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_4\\
\frac{dx_5}{dt}&=f_5=\left(\alpha_A x_5+\alpha_C x_7\right)x_2-k_4x_5\\
&\quad+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_5\\
\frac{dx_6}{dt}&=f_6=\sigma_A\varphi_U x_4-k_5x_6\\
&\quad+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_6\\
\frac{dx_7}{dt}&=f_7=\sigma_A\varphi_F x_5+\sigma_C x_6-k_6x_7\\
&\quad+\left(\delta_A\left(x_4+x_5\right)+\delta_C x_7\right)x_7
\end{aligned} \qquad \textbf{(18)}$$

Now, the Jacobian of the system (3.18) above at the disease free equilibrium (which is the same as the Jacobian of (3.13)) is given by:

$$J(E_f)=\begin{pmatrix} -K_1 & 0 & 0 & \delta_A x_1^* & -b_A+\delta_A x_1^* & 0 & -b_C+\delta_C x_1^* \\ \sigma_S & -K_2 & \omega & \delta_A x_2^* & -(\alpha_A-\delta_A)x_2^* & 0 & -(\alpha_C-\delta_C)x_2^* \\ \rho_U & \rho_F & -K_3 & \delta_A x_3^* & \delta_A x_3^* & 0 & \delta_C x_3^* \\ 0 & 0 & 0 & -K_4 & b_A & 0 & b_C \\ 0 & 0 & 0 & 0 & \alpha_A x_2^* - K_4 & 0 & \alpha_C x_2^* \\ 0 & 0 & 0 & \sigma_A\varphi_U & 0 & -K_5 & 0 \\ 0 & 0 & 0 & 0 & \sigma_A\varphi_F & \sigma_C & -K_6 \end{pmatrix} \quad \textbf{(19)}$$

from which it has been shown in (8) that the effective basic reproduction number, R_C is given by:

$$R_C=\frac{\alpha_A x_2^*}{K_4}\left(1+\frac{\eta\sigma_A(K_4K_5\varphi_F+\sigma_C\varphi_U b_A)}{(K_4K_5K_6-\sigma_C\sigma_A\varphi_U b_C)}\right)$$

Consider the case when $R_C=1$. Suppose, further, that $\alpha_A=\alpha^*$ is chosen as a bifurcation parameter, since R_C is often inconvenient to use directly as bifurcation parameter. Solving for α_A gives $R_C=1$ when,

$$\alpha_A=\alpha^*=\frac{K_4}{x_2^*\left(1+\frac{\eta\sigma_A(K_4K_5\varphi_F+\sigma_C\varphi_U b_A)}{(K_4K_5K_6-\sigma_C\sigma_A\varphi_U b_C)}\right)} \quad \textbf{(20)}$$

Let V and W be the corresponding left and right eigenvectors associated with the zero eigenvalues of the Jacobian of (19) at $\alpha_A=\alpha^*$ (denoted by J_{α^*}) chosen such that $VJ(E_0)=0$ and $J(E_0)W=0$ with $VW=1$, where $V=[v_1,v_2,v_3,v_4,v_5,v_6,v_7]$, and $W=[w_1,w_2,w_3,w_4,w_5,w_6,w_7]^T$. Thus,

$$VJ(E_f)=[v_1,v_2,v_3,v_4,v_5,v_6,v_7]\times\begin{pmatrix} -K_1 & 0 & 0 & \delta_A x_1^* & -b_A+\delta_A x_1^* & 0 & -b_C+\delta_C x_1^* \\ \sigma_S & -K_2 & \omega & \delta_A x_2^* & -(\alpha_A-\delta_A)x_2^* & 0 & -(\alpha_C-\delta_C)x_2^* \\ \rho_U & \rho_F & -K_3 & \delta_A x_3^* & \delta_A x_3^* & 0 & \delta_C x_3^* \\ 0 & 0 & 0 & -K_4 & b_A & 0 & b_C \\ 0 & 0 & 0 & 0 & \alpha_A x_2^* - K_4 & 0 & \alpha_C x_2^* \\ 0 & 0 & 0 & \sigma_A\varphi_U & 0 & -K_5 & 0 \\ 0 & 0 & 0 & 0 & \sigma_A\varphi_F & \sigma_C & -K_6 \end{pmatrix}=\begin{pmatrix}0\\0\\0\\0\\0\\0\\0\end{pmatrix}$$

Solving, gives

$$v_1=0,\ v_2=0,\ v_3=0, v_4=\frac{\sigma_A\varphi_U\sigma_U v_7}{K_4K_5}\ v_5=\frac{(b_A\sigma_A\varphi_U\sigma_U+K_4K_5\sigma_A\varphi_F)v_7}{K_4K_5(K_4-\alpha_A x_2^*)}$$

$$v_6=\frac{\sigma_C v_7}{K_5}, v_7>0 \text{ (can take any value)}$$

Similarly,

$$J(E_f)W=\begin{pmatrix} -K_1 & 0 & 0 & \delta_A x_1^* & -b_A+\delta_A x_1^* & 0 & -b_C+\delta_C x_1^* \\ \sigma_S & -K_2 & \omega & \delta_A x_2^* & -(\alpha_A-\delta_A)x_2^* & 0 & -(\alpha_C-\delta_C)x_2^* \\ \rho_U & \rho_F & -K_3 & \delta_A x_3^* & \delta_A x_3^* & 0 & \delta_C x_3^* \\ 0 & 0 & 0 & -K_4 & b_A & 0 & b_C \\ 0 & 0 & 0 & 0 & \alpha_A x_2^* - K_4 & 0 & \alpha_C x_2^* \\ 0 & 0 & 0 & \sigma_A\varphi_U & 0 & -K_5 & 0 \\ 0 & 0 & 0 & 0 & \sigma_A\varphi_F & \sigma_C & -K_6 \end{pmatrix}\begin{pmatrix} w_1 \\ w_2 \\ w_3 \\ w_4 \\ w_5 \\ w_6 \\ w_7 \end{pmatrix}=\begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

and solving, we have,

$$w_1=\frac{\left\{\begin{array}{l}\delta_A x_1^*\left\{\begin{array}{l}b_A\alpha_C x_2^* \\ +b_C\left(K_4-\alpha_A x_2^*\right)\end{array}\right\} \\ -K_4\left(b_A-\delta_A x_1^*\right)\alpha_C x_2^* \\ -K_4\left(K_4-\alpha_A x_2^*\right)\left(b_C-\delta_C x_1^*\right)\end{array}\right\}w_7}{K_1K_4\left(K_4-\alpha_A x_2^*\right)}$$

$$w_2=\frac{\left\{\begin{array}{l}\sigma_S w_1+\delta_A x_2^* w_4-(\alpha_A-\delta_A)x_2^* w_5 \\ -(\alpha_C-\delta_C)x_2^* w_7\end{array}\right\}}{K_2}$$

$$+\frac{\omega\left\{\begin{array}{l}(K_2\rho_U+\rho_F\sigma_S)w_1 \\ +\left(K_2\delta_A x_3^*+\rho_F\delta_A x_2^*\right)w_4 \\ +\left(K_2\delta_A x_3^*-\rho_F(\alpha_A-\delta_A)x_2^*\right)w_5 \\ +\left(K_2\delta_C x_3^*-\rho_F(\alpha_C-\delta_C)x_2^*\right)w_7\end{array}\right\}}{K_2(K_2K_3-\rho_F\omega)}$$

$$w_3=\frac{\left\{\begin{array}{l}(K_2\rho_U+\rho_F\sigma_S)w_1 \\ +\left(K_2\delta_A x_3^*+\rho_F\delta_A x_2^*\right)w_4 \\ +\left(K_2\delta_A x_3^*-\rho_F(\alpha_A-\delta_A)x_2^*\right)w_5 \\ +\left(K_2\delta_C x_3^*-\rho_F(\alpha_C-\delta_C)x_2^*\right)w_7\end{array}\right\}}{(K_2K_3-\rho_F\omega)}$$

$$w_4=\frac{\left\{b_A\alpha_C x_2^*+b_C\left(K_4-\alpha_A x_2^*\right)\right\}w_7}{K_4\left(K_4-\alpha_A x_2^*\right)},$$

$$w_5=\frac{\alpha_C x_2^* w_7}{\left(K_4-\alpha_A x_2^*\right)}$$

$$w_6=\frac{\sigma_A\varphi_U\left\{b_A\alpha_C x_2^*+b_C\left(K_4-\alpha_A x_2^*\right)\right\}w_7}{K_4K_5\left(K_4-\alpha_A x_2^*\right)}$$

$w_7>0$ (can take any value)

Computation of a and b :

For a , we have

$$a=\sum_{k,i,j=1}^{n}v_k w_i w_j\frac{\partial^2 f_k}{\partial x_i\partial x_j}(0,0)$$

Computing the associated non-zero partial derivatives of F at the DFE for the sign of a we have:

$$a=2\left\{\begin{array}{l}v_4w_4w_4\delta_A+v_5w_5\left(w_5\delta_A+w_7\delta_C\right) \\ +v_7w_7w_5\delta_A+v_4w_4\left(w_5\delta_A+w_7\delta_C\right) \\ +v_5w_2\left(w_5\alpha_A+w_7\alpha_C\right)+v_5w_5w_4\delta_A \\ +v_6\left(w_4w_5\delta_A+w_5w_6\delta_A+w_6w_7\delta_C\right) \\ +v_7w_7\left(w_4\delta_A+w_6\delta_C\right)\end{array}\right\}>0$$

Similarly, for b , we have

$$b=\sum_{k,i=1}^{n}v_k w_i\frac{\partial^2 f_k}{\partial x_i\partial\phi}(0,0)$$

And thus, computing the associated non-zero partial derivatives of F at the DFE for the sign of b we have:

$$b = x_2^* > 0$$

Thus we established the following result.

Theorem 5: the model (3.4) exhibit a subcritical (backward) bifurcation at $\alpha^* = 0$.

By occurrence of backward bifurcation, it means that for $R_C < 1$, a stable disease free-equilibrium coexists with two endemic equilibria: a smaller equilibrium (i.e., with a smaller number of infective individuals) which is stable and a larger one (i.e., with a larger number of infective individuals) which is stable. These two endemic equilibria disappear by saddle node bifurcation when the effective basic reproduction number, R_C is decreased below the critical values $R_C^{sn} < 1$. And for $R_C > 1$, there are only two equilibria: the disease free-equilibrium, which is unstable, and the larger endemic equilibrium, which is stable (Buonomo and Lacitignola). Thus, it is highly remarkable that $R_C^{sn} < 1$ is a necessary and sufficient condition for disease control (elimination) and while $R_C < 1$ is only a necessary condition.

RESULTS AND DISCUSSION

In this section, we presented some numerical simulation to monitor the dynamics of the full model (1) for various values of the associated effective basic reproduction number in order to confirm our analytical results on the global stability of the disease free-equilibrium, occurrence of a backward bifurcation as well as effect of different control strategies. Parameter values based on HBV epidemiological and published data studies shown in table 1 below as
in Abdulrahman et al., (2012) are used for the simulations.

Table 1: Baseline Values for Parameters for the Model (1).

S/N	Parameter	Baseline Value	S/N	Parameter	Baseline Value
1	b	0.036	11	φ_U	0.885
2	μ	0.021	12	φ_F	0.1
3	p	0.6	13	γ_{CF}	0.015
4	c	3.233	14	δ_A	0.0007
5	η	0.667	15	δ_C	0.00131
6	θ	0.724	16	ε_ρ	0.9
7	ϕ	0.159	17	ω	0.04
8	σ_S	0.0667	18	ε_c	0.8
9	σ_A	2.667	19	$\tau_b, \tau_U, \tau_F, \tau_c$	(0-1)
10	σ_C	0.069			

Threshold Simulations: Figure 1 confirms the global asymptotic stability of the endemic equilibrium, with the persistence of the solution profiles for $R_C = 1.775$ and different initial conditions for the variables. Figure 2 illustrate the backward bifurcation phenomenon of the model, with the persistence of the disease despite the effective basic reproduction numbers, R_C are less than one. And with $R_C^{sn} = 0.154$, using same variables as in Figure 1, we clearly see in Figure 3 that the solution profiles converges to the disease free equilibrium in all cases which confirms our analytical result of global asymptotical stability of disease free equilibrium.

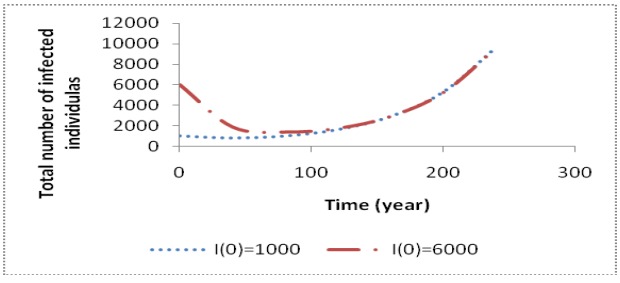

Figure 1: Total Number of Infected Individuals with Different Initial Variables Conditions (i.e., $I(0) = 1000$ and $I(0) = 6000$). (Control parameters used are $\tau_b = \tau_U = \tau_F = 0$ and $\tau_c = 0.25$ which gives $R_C = 1.775$).

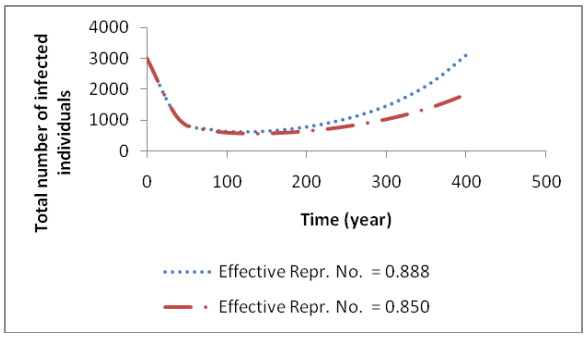

Figure 2: Total Number of Infected Individuals with Two Different Effective Basic Reproduction Numbers which are less than unity (i.e., $R_C = 0.888$ and $R_C = 0.850$.) (Control parameters used are $\tau_b = \tau_U = \tau_F = 0$ $\tau_c = 0.75$ and $\tau_b = 0.25, \tau_U = \tau_F = 0, \tau_c = 0.75$, respectively.

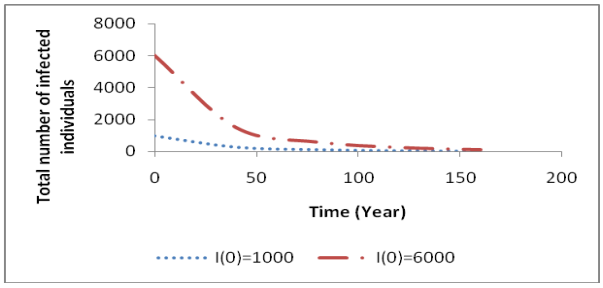

Figure 3: Total Number of Infected Individuals with Different Initial Variable Conditions (i.e., $I(0) = 1000$ and $I(0) = 6000$). (Control parameters used are $\tau_b = \tau_U = \tau_F = 0$, and $\tau_c = 0.5$, which gives $R_C = 0.154$).

Effect of Control Strategies

The full model is simulated to assess the effect of compliance to condom usage and 3 different vaccination strategies (τ_c, τ_b, τ_U, and τ_F) as follows:

a) No Control: Figure 4 illustrates the situation in which there is no control. The infected individuals are increasing.

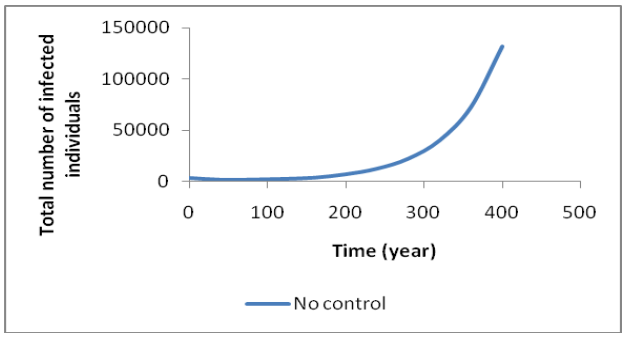

Figure 4: Total Number of Infected Individuals without any Control Measures. (Control parameters used are $\tau_b = \tau_U = \tau_F = \tau_c = 0$, which gives $R_C = 2.219$).

b) Single Strategies: Here simulations are carried out to monitor the impact of 3 different levels (low, moderate and high) of each of the 4 control strategies. Figure 5 reveals that τ_c only at any level cannot eliminate the disease as it resulted in endemic state or backward bifurcation. Both τ_b, and τ_U controls at all the 3 levels show disease persistence and thus, not enough for disease elimination as illustrated in Figures 6 and 7 respectively. The τ_F control any of the 3 levels shows convergence of the solutions to disease free-equilibrium as depicted in Figure 8.

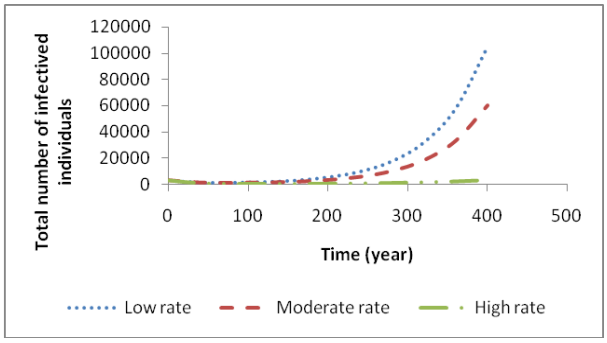

Figure 5: Total Number of Infected Individuals with respect to the 3 Different Levels of τ_c only. (Control parameters used are $\tau_b = \tau_U = \tau_F = 0$ and $\tau_c = 0.25, 0.5, 0.75$ respectively, for the 3 control levels which give $R_C = 1.775$ for low levels, $R_C = 1.775$ for moderate levels, and $R_C = 0.888$ for high levels).

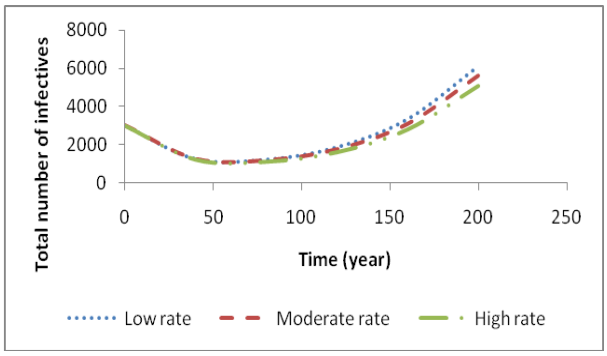

Figure 6: Total Number of Infected Individuals with Respect to the 3 Different Levels of τ_b only. (Control Parameters used are $\tau_U = \tau_F = \tau_c = 0$ and $\tau_b = 0.25, 0.5, 0.75$, respectively, for the 3 control levels which give $R_C = 2.124$ for low levels, $R_C = 2.030$ for moderate levels, and $R_C = 1.935$ for high levels).

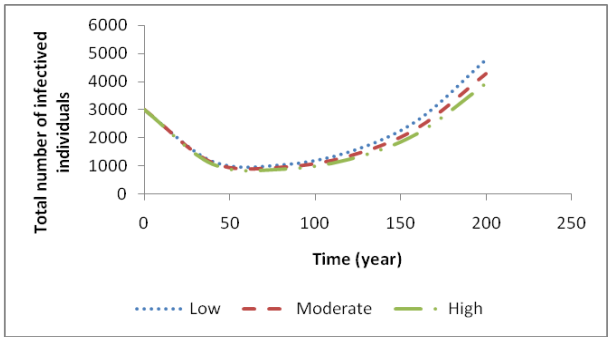

Figure 7: Total Number of Infected Individuals with Respect to the 3 different levels of τ_U only. (Control parameters used are $\tau_b = \tau_F = \tau_c = 0$ and $\tau_U = 0.25, 0.5, 0.75$, respectively, for the 3 control levels which give $R_C = 1.912$ for low levels, $R_C = 1.841$ for moderate levels, and $R_C = 1.801$ for high levels).

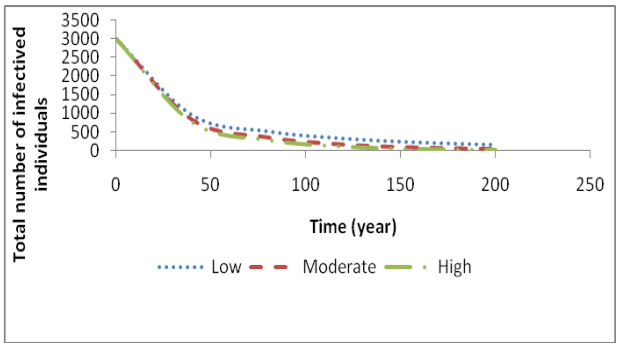

Figure 8: Total Number of Infected Individuals with Respect to the 3 Different Levels of τ_F only. (Control parameters used are $\tau_b = \tau_U = \tau_c = 0$ and $\tau_F = 0.25, 0.5, 0.75$, respectively, for the 3 control levels which give $R_C = 0.556$ for low levels, $R_C = 0.315$ for moderate levels, and $R_C = 0.219$ for high levels).

c) Combined Strategies: Here simulations are carried out to monitor the impact of the 3 different levels (low, moderate, and high) of the 4 combined control strategies. Figure 9 shows convergence of the solutions to disease free equilibrium for even a low level of the combine strategies.

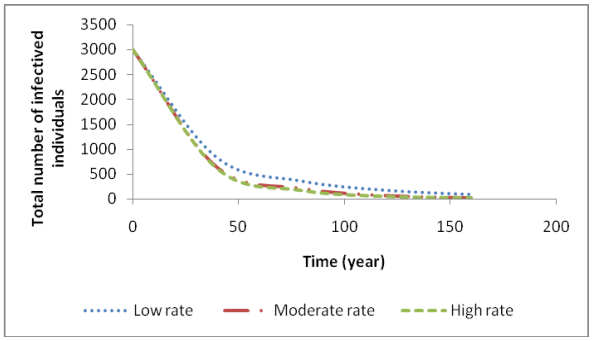

Figure 9: Total Number of Infected Individuals with Respect to the 3 Different levels of Combined 4 Controls. (Control Parameters Levels used are $0.25, 0.5, 0.75$ which give, respectively, for the 3 control levels, $R_C = 0.377$ for low levels, $R_C = 0.154$ for moderate levels, and $R_C = 0.070$ for high levels).

CONCLUSION

In this paper, we have presented a mathematical model which incorporated very important factors which plays significant role in the transmission dynamics and control of HBV. These factors are; Vital dynamics, vertical transmission, public enlightenment, condom usage, standard incidence, disease induced death due to both acute and chronic infection, waning of immunization and sexual maturity. Our analysis reveals that the disease can be control if the effective basic reproduction number, R_C is less than one and also the existence of backward bifurcation which can be attributed to the effect of waning of vaccination.

Furthermore, our analysis reveals that childhood HBV vaccination alone cannot control (eliminate) the disease. Instead public enlightenment on HBV vaccination should target more of those individuals that are sexually active (fifteen years and above). Though, universal (combine) controls is the best strategy for controlling HBV disease.

REFERENCES

1. Abulrahman, S., N.I. Akinwande, O.B. Awojeyegbe, and U.Y. Abubakar. 2012. "Mathematical Solution for Hepatitis B Virus Elimination in Nigeria". *Journal of Pure and Applied Sciences*. 11(1):27 – 30.

2. Adeoye, G. 2010. "Twenty million Nigerians at Risk from Hepatitis B". Retrieved from http://www.plurpol.org/joom/index.php/regional-news/64-africa/6245.

3. Akinwande, N.I. 1996. "A Mathematical Model of Yellow Fever Epidemics". *Afrika Matematika Serie*. 3(6):49 – 59.

4. Benyah, F. 2008. *Introduction to Epidemiological Modeling*. 10th Regional College on Modeling Simulation and Optimization. University of Cape Coast: Ghana.

5. Buonomo, B. and D. Lacitignolu. 2011. "On the Backward Bifurcation of a Vaccination Model with Non-Linear Incidence". *Non-linear Analysis: Modelling and Control*. 16(1):30 – 46.

6. Busenberg, S., K. Cooke, and M. Iannelli. 1990. Analysis of a Disease Transmission Model in a Population with Varying Size". *J. Math. Biol*. 28: 257-270.

7. Capasso, V. 2008. "Mathematical Structures of Epidemic System". In: Levin, S. A. (ed). *Lecture Notes in Biomathematics*. 97. Springer-Verlag: Berlin, Germany.

8. Castillo-Chavez, C., Z. Feng, and W. Huang. 2002. "On the Computation of R0 and its Role on Global Stability". In: Castillo-Chavez C., Blower S., Van den Driessche P., Krirschner D. and Yakubu A. A. (eds.). *Mathematical approaches for emerging and reemerging infectious diseases: An introduction. The IMA volumes in mathematics and its applications*. Springer Verlag: New York, NY. 125:229-250.

9. Castillo-Chavez, C. and B. Song. 2004. "Dynamical Model of Tuberculosis and Their Applications". *Mathematical Biosciences and Engineering*. 1:361-404.

10. Dahari, H., E. Shudo, R.M. Ribeiro, and A.S. Perelson. 2009. "Modelling Complex Decay Profiles of Hepatitis B Virus During Antiviral Therapy". *Hepatology*. 49(1):32-38.

11. Diekmann, O. and A. Heesterbeek. 2000. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Integration*. John Wiley and Sons: New York, NY.

12. Fall, A., A. Iggidr, G. Sallet, and J. Tewa. 2007. "Mathematical Modelling of Natural Phenomena". *Epidemiology*. 2(1): 55 – 73.

13. Garba, S.M. and A.B. Gumel. 2010. "Mathematical Recipe for HIV Elimination in Nigeria". *Journal of the Nigeria Mathematical Society*. 29:51-112.

14. Hethcote, H.W. 2000. "The Mathematics of Infectious Diseases". *SIAM Review*. 42(4):599-653.

15. Hoofnagle, J.H., E. Doo, T.J. Liang, R. Fleischer and A.S.F. Lok. 2007. "Management of Hepatitis B: Summary of a Clinical Research Workshop". *Hepatology*, 45:1056 – 1075.

16. Huo, H.F.., S.J. Dang, and Y.N. Li. 2010. "Stability of a Two-Strain Tuberculosis Model with General Contact Rate". *Abstract and Applied Analysis.* ID 293747. Doi: 10.1155/2010/293747.

17. Kaplan, E. and M. Brandeau. 1994. *Modelling AIDS and the AIDS Epidemic*. Raven: New York, NY.

18. Li, M.Y., J.R. Graef, L. Wang, and J. Karsai. 1999. "Global Stability for the SEIR Model with Varying Total Population Size". *Mathematical Biosciences*.160:191-213.

19. Long, C., H. Qi, and S.H. Huang. 2008. "Mathematical Modelling of Cytotoxic Lymphocyte– Mediated Immune Response to Hepatitis B Virus Infection". *J. of Biomedicine and Biotechnology*. Published online, PMCID: PMC2246092: 1 – 18

20. Ma, J. and Z. Ma. 2006. "Epidemic Threshold Conditions for Seasonally Forced SEIR Models". *Journal of Mathematical Biosciences and Engineering*. 3(1):161 – 172.

21. Medley, G.F., N.A. Lindop, W.J. Edmunds, and D.J. Nokes. 2001. "Hepatitis B Virus Endemicity: Heterogeneity, Castastrophic Dynamics and Control". *Nature Medicine*. 7(5):619-24.

22. Pasquini, P., N. Delimar, M. Kosicek, R. De Blasio, R. Raschetti, and B. Evjetanovic. 1987. "Impact of Hepatitis B Immunization Strategies on Infection Rates in Italy: A Deterministic Computer Simulation". *Eur. J. Epidemiol*. 3(1):19-24.

23. Scherer, A. and A. Mclean. 2002. "Mathematical Models of Vaccination". *British Medical Bulletin*. 62:187-199.

24. Sutton, A.J., N.J. Gay, and W.J. Edmunds. 2006. "Modelling the Impact of Prison Vaccination on Hepatitis B Transmission within the Injecting Drug User Population of England and Wales". *Vaccine*. 24:2377 - 2386.

25. Thorney, S., C. Bullen, and M. Robbert. 2008. "Hepatitis B in High Prevalence New Zeeland Population: A Mathematical Model Applied to Infection Control Policy". *J. Theo Bio*. 254(30):599-603.

26. Tumwiine, J. et al. 2007. "A Mathematical Model for the Dynamics of Malaria in Human Host and Mosquito Vector with Temporary Immunity". *Appl. Mathematics and Computation*. 189:1953 – 1965.

27. Williams, J. R., D,J. Nokes, G.F. Medley, and R.M. Anderson. 1996. "The Transmission Dynamics of Hepatitis B in the UK: A Mathematical Model for Evaluating Costs and Effectiveness of Immunization Programmes". *Epidemiol Infect*. 116(1):71-89.

28. Williams, R. 2006. "Global Challenges in Liver Disease". *Hepatology*. 44(3):521 – 526.

29. WHO (World Health Organization). 2009. *Hepatitis B*. Fact Sheet No. 204. http.//www.who.int/mediacentre/factsheets/fs204/en/ (accessed December 12, 2008).

30. Zhao, S., Z. Xu, and Y. Lu. 2000. "A Mathematical Model of Hepatitis B Virus Transmission and its Application for Vaccination Strategy in China". *International Journal of Epidemiology*. 29(14):744-752.

31. Zou, L., W. Zhang, and S. Ruan. 2010. "Modelling the Transmission Dynamics and Control of Hepatitis B Virus in China". *J of Theor Biol*. 262:330-338.

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