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Stability Analysis of Mathematical Model of Hepatitis B Dynamics with Vaccination, Treatment and Post-Exposure Prophylaxis

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ABSTRACT

According to WHO, about 296 million people live with chronic hepatitis B infection and this hepatitis B can lead to death through cirrhosis-induced liver failure. In this paper, the stability analysis of both disease-free and endemic equilibrium of the SEACVR model for the transmission of hepatitis B was studied in the sense of Lyapunov. The study used the Variable gradient method and the Krascosvii method of constructing the Lyapunov function to construct the Lyapunov function of the model. The study performed a numerical simulation to confirm the definiteness of the constructed Lyapunov function.

Keywords: Stability, Lyapunov, Definiteness, Variable gradient, Reproduction number

1. Introduction

Hepatitis B is still one of the biggest challenges faced by humanity in terms of infectious diseases. There are two major phases of HBV infection, the acute and chronic phase: The acute infection stays up to six months and the infected individual recovers or becomes a chronic carrier of the HBV. The acute infection is identified by the presence of HBcAg, and HBc – IgM antibodies and may last for six months and progress to the Chronic phase when the presence of HBsAg persists longer than 6 months (Lok et al. 2004).

Hepatitis B Virus is very dangerous to humans; this is because it affects the liver, thereby restraining the function of the vital organ. The vaccination for HBV infection is made up of two kinds, plasma-derived vaccines and recombinant vaccines. These two show no differences in terms of duration of protection and effectiveness. The former is prepared from purified HBsAg obtained from the plasma of persons with chronic HBV infection. Post-exposure prophylaxis (PEP) can help to treat an infection and prevent the subsequent development of a chronic infection or liver disease for uninfected, unvaccinated persons or anyone who does not know their hepatitis B status that is exposed to the hepatitis B virus through contact with infected blood (CDC, 2020). High HBV presence is common in much of mid-Asia; West Africa, East Africa, Central Asia and East Asia have up to 5% - 8% of the population living with hepatitis B virus (CDC, 2020).

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. Understanding the transmission characteristics of infectious diseases in communities, regions and countries in a mathematical framework can lead to better approaches to decreasing the transmission of these diseases (Anderson and May, 1991). In other words, Mathematical models are tools that help to capture infection or disease transmission mechanisms or dynamics in a population in the form of a mathematical framework to predict the behaviour of the disease spread through the population.

Stability is one of the most important properties of a system. Stability is referred to the ability of any object to return to its original position after it has been tilted slightly. In terms of a system, it is referred to as the ability of the system to perform adequately or the ability of a system to return to its equilibrium point after a slight perturbation. There are different types of stability and the most significant one is the stability of solutions near an equilibrium point (Lyapunov A.M, 1992).

Lyapunov theory is used to establish local and global stability for epidemiological classes. Nayeem et al (2014) after studying Zou et al.'s model, developed a deterministic model $XYLICR$ to understand the underlying dynamics of HBV infection at the population level (X – susceptible individual, Y - vaccinated individuals, L – infected but not yet infectious, I – acutely infected individuals, C – chronic HBV carriers and R –acquiring treatment recovered individuals). They showed that in the absence of such re-infection, the model has a disease-free equilibrium (DFE) which is globally asymptotically stable (GAS), using the Lyapunov function and LaSalle Invariance Principle whenever the associated reproduction threshold is less than unity.

Aniji et al (2020) studied approximate solutions for HBV infection with stability analysis using Liao's homotopy analysis method (LHAM). examine the basic nonlinear deferential equation by LHAM to get a semi-analytical solution. They determined that their model is the local and global stability disease-free and endemic equilibrium by using the Lyapunov function

Akbari et al (2016) presented a five compartments model $SEICR$, they took into account that there are newly born who is born immune, susceptible get vaccinated which wanes after some time and that an individual who is carrier recovers naturally without drug treatment or with drug treatment. they analysed the local stability of the disease-free equilibrium which follows from the Routh-Hurwitz criterion that the eigenvalues have negative real parts if the basic reproduction number is less than one and hence established that the disease-free equilibrium of the model is local asymptotically stable if the basic reproduction number is less than one and unstable if the basic reproduction number is greater s than one. They stated that if $R_0 < 1$, then the disease-free equilibrium is globally stable and the disease always dies out and if $R_0 > 1$, the disease-free equilibrium is unstable and the disease is uniformly persistent.

2. The Model

The study presents the SEACVR model by Ogbuagu et al (2023) basic properties of mathematical model of hepatitis b dynamics with vaccination, treatment and post exposure prophylaxis. The model incorporates the intervention measures i.e., vaccination, treatment and Post Exposure Prophylaxis (PEP) of Hepatitis B. The model consists of Susceptible $S(t)$ Exposed $E(t)$, Acute infected $A(t)$, Chronic carrier infections $C(t)$, vaccinated $V(t)$ and Recovered $R(t)$.

The total population of S, E, A, C, V, R at time t is $N(t)$, and

$$N(t) = S(t) + E(t) + A(t) + C(t) + V(t) + R(t) \quad (1)$$

Individuals are recruited into the population at the constant rat B. The susceptible population increases by the recruitment of individuals who are not vaccinated at the rate $B\omega_0$, where ω_0 is the proportion of non-vaccinated recruitment, while the complementary proportion $(1-\omega_0)B$ is protected, that is vaccinated and enter the class of vaccinated individuals V. The susceptibility decreases due to HBV infection at rate λS, where λ in the force of infection given by

$$\lambda = \frac{\beta(A+\varepsilon C)}{N} \quad (2)$$

where β is the transmission coefficient of HBV and $0 < \varepsilon < 1$ is a modification parameter that takes into account the fact that acute are most infectious than chronic HBV.

The population of vaccinated individuals increased by the vaccination of the newborn babies at the rate $(1-\omega_0)B$ and vaccination of susceptible individuals at a constant rate γ_3. Since the vaccination does not confer permanent immunity to all vaccine recipients, vaccinated individuals lose their immunity when the vaccine wanes and return to the susceptible class S at a constant rate φ.

After being exposed to the infection, the individual move to the exposed class. Exposed individuals who are aware of being exposed take the post-exposure vaccine and move to the vaccinated class at the rate γ_2, while those who are not aware become infectious and move from exposure class to acutely infected class at a constant rate of σ. γ_1 is the rate at which individuals leave the acutely infected class, q is the proportion that leaves acute and progresses to chronic class and $1-q$ is the proportion that leaves the acutely infected class and progresses to recovered when treated. At the rate of α, individuals leave the chronic class to recover when treated or move to the recovered class at the rate of θ when HBV is naturally cleared without treatment. Exit from the population is by natural and HBV- related mortality only at the rate μ_0 and μ_1 respectively

2.2 The Model Equation

The model consists of the following ordinary differential equations (ODE)

$$\begin{aligned}
S' &= Bw_0 + \varphi V - (\lambda + \gamma_3 + \mu_0)S \\
E' &= \lambda S - (\gamma_2 + \mu_0 + \sigma)E \\
A' &= \sigma E - (\mu_0 + \gamma_1)A \quad (3) \\
C' &= q\gamma_1 \mathrm{A} - (\mu_0 + \mu_1 + \alpha + \theta)C \\
V' &= B(1-w_0) + \gamma_3 S + \gamma_2 E - (\mu_0 + \varphi)V \\
R' &= (1-q)\gamma_1 A + (\alpha + \theta)C - \mu_0 R
\end{aligned}$$

3.1 The Disease-Free Equilibrium

Here the study considered the case of a population at the time of eradicating HBV. The disease-free equilibrium (DFE) for an epidemiological model is an equilibrium such that the disease is absent in the community.

Thus,

Let $D_0 = (S_0, E_0, A_0, C_0, V_0, R_0)$ is the DFE of model system (3),

then $E_0 = A_0 = C_0 = 0$. As a consequence of model system (3), $R_0 = 0$ with S_0 and V_0 being solutions of the system:

$S_0' = Bw_0 + \varphi V_0 - (\gamma_3 + \mu_0)S_0 = 0$

$V_0' = B(1 - w_0) + \gamma_3 S_0 - (\mu_0 + \varphi)V_0 = 0$

This has a unique solution:

$S_0 = \frac{B(\varphi+\omega_0\mu_0)}{\mu_0(\mu_0+\varphi+\gamma_3)}$, $V_0 = \frac{B(\mu_0(1-\omega_0)\gamma_3)}{\mu_0(\mu_0+\varphi+\gamma_3)}$ and $N_0 = S_0 + V_0 = \frac{B}{\mu_0}$. (4)

3.2 Endemic Equilibrium

In this section, we compute the model endemic equilibrium point G^*. This is done by setting the differential equations of the model system (3) equal to zero. The endemic equilibrium is given by

$G^* = [S^*, E^*, A^*, C^*, V^*, R^*]$, at steady state $S', E', A', C', V', and\ R'$

That is

$S' = Bw_0 + \varphi V - (\lambda + \gamma_3 + \mu_0)S = 0$

$E' = \lambda S - (\gamma_2 + \mu_0 + \sigma)E = 0$

$A' = \sigma E - (\mu_0 + \gamma_1)A = 0$

$C' = q\gamma_1 - (\mu_0 + \mu_1 + \alpha + \theta)C = 0$

$V' = B(1 - w_0) + \gamma_3 S + \gamma_2 E - (\mu_0 + \varphi)V = 0$

$R' = (1 - q)\gamma_1 A + (\alpha + \theta)C - \mu_0 R = 0$

From the above system of equations (3), we have

$S = \frac{Bw_0+\varphi V}{(\lambda+\gamma_3+\mu_0)}$

$E = \frac{\lambda S}{(\gamma_2+\mu_0+\sigma)}$

$A = \frac{\sigma E}{\mu_0+\gamma_1}$

$C = \frac{q\gamma_1 A}{(\mu_0+\mu_1+\alpha+\theta)}$

$V = \frac{B(1-w_0)+\gamma_3 S+\gamma_2 E}{\mu_0+\varphi}$

$R = \frac{(1-q)\gamma_1 A+(\alpha+\theta)C}{\mu_0}$

Substitute $E = \frac{\lambda S}{(\gamma_2+\mu_0+\sigma)}$ in $V = \frac{B(1-w_0)+\gamma_3 S+\gamma_2 E}{\mu_0+\varphi}$, we have that

V = $\frac{B(1-w_0)+\gamma_3 S+\gamma_2\left(\frac{\lambda S}{(\gamma_2+\mu_0+\sigma)}\right)}{\mu_0+\varphi}$,

substituting this V in the first equation of the model of the endemic equilibrium, that is

$S^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$ (5)

Substituting $S^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$ in E^* below, we have

$E^* = \left(\frac{\lambda S^*}{(\gamma_2+\mu_0+\sigma)}\right) = \left(\frac{\lambda(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right)$ (6)

Substituting $S^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$ in A^* below, we have

$A^* = \left(\frac{\lambda\sigma(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right)$ (7)

Substituting $S^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$ in C^* below, we have that

$C^* = \left(\frac{q\gamma_1\lambda\sigma S^*}{(\gamma_2 + \mu_0 + \sigma)(\mu_0 + \gamma_1)(\mu_0 + \mu_1 + \alpha + \theta)}\right)$

$$= \left(\frac{q\gamma_1\lambda\sigma(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)(\mu_0+\mu_1+\alpha+\theta)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right) \quad (8)$$

$$V^* = \frac{B(1-w_0) + \gamma_3 S^* + \gamma_2 E^*}{\mu_0 + \varphi}$$

Substituting $s^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$

and

$E^* = \left(\frac{\lambda(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right)$ in V^* below, we have

$$V^* = \frac{B(1-w_0)}{\mu_0+\varphi} + \gamma_3\left(\frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}\right) + \gamma_2\left(\frac{\lambda(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right) \quad (9)$$

$$R^* = \frac{(1-q)\gamma_1 A^* + (\alpha+\theta)C^*}{\mu_0}$$

Substituting $s^* = \frac{Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma)}{(\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi}$

and $C^* as$

$$\left(\frac{q\gamma_1\lambda\sigma(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)(\mu_0+\mu_1+\alpha+\theta)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right)$$

$$R^* = \left(\frac{(1-q)\gamma_1}{\mu_0}\right)\left(\frac{\lambda\sigma(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right)$$
$$+\left(\frac{(\alpha+\theta)}{\mu_0}\right)\left(\frac{q\gamma_1\lambda\sigma(Bw_0(\mu_0+\varphi)+B(1-w_0)(\gamma_2+\mu_0+\sigma))}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)(\mu_0+\mu_1+\alpha+\theta)((\lambda+\gamma_3+\mu_0)(\mu_0+\varphi)-(\gamma_3(\gamma_2+\mu_0+\sigma)+\gamma_2\lambda)\varphi)}\right) \quad (10)$$

Hence, the above equation shows that the endemic equilibrium exists.

The study define the basic reproduction number, R_0 as the largest eigenvalue of the next generation matrix FV^{-1}. Thus,

$$R_0 = \frac{\sigma S_0\beta((\mu_0+\mu_1+\alpha+\theta)+\varepsilon q\gamma_1)}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)(\mu_0+\mu_1+\alpha+\theta)N_0} \quad (11)$$

Theorem 1 The disease-free equilibrium of the model without delay system 3 is locally asymptotically stable if $R_0 < 1$

Proof

Consider an autonomous system

$$x' = f(x,t) \quad (12)$$

We need to construct a Lyapunov function V such that $V(x)$ is positive definite i.e., $V(x) > 0$

$\forall\, x$and $V'(x)$ is negative definite that is $V'(x) \leq 0\ \forall\, x \in \Omega$.

Using the variable gradient method and taking into account of the disease-free equilibrium where we have that

$S' = Bw_0 + \varphi V_0 - (\mu_0 + \gamma_3)S_0 = 0$

$V' = B(1-w_0) + \gamma_3 S_0 - (\mu_0 + \varphi)V_0 = 0$

Let $S_0 = x_1, V_0 = x_2$

we let ∇V be n undetermined component and $V(x)$ be the lyapunov function

then we have that

$$V'(x) = \frac{d\nabla V(x)}{dx} = \frac{\partial V}{\partial x_1}\frac{\partial x_1}{\partial t} + \frac{\partial V}{\partial x_2}\frac{\partial x_2}{\partial t} + \frac{\partial V}{\partial x_3}\frac{\partial x_3}{\partial t} + \cdots + \frac{\partial V}{\partial x_n}\frac{\partial x_n}{\partial t}$$
$$= \nabla V_1\frac{\partial x_1}{\partial t} + \nabla V_2\frac{\partial x_2}{\partial t} + \nabla V_3\frac{\partial x_3}{\partial t} + \cdots + \nabla V_n\frac{\partial x_n}{\partial t}$$

Therefore, $V'(x) = (\nabla V)^T x'$

Where $\nabla V = \begin{bmatrix} \frac{\partial V}{\partial x_1} \\ \frac{\partial V}{\partial x_2} \\ \vdots \\ \frac{\partial V}{\partial x_n} \end{bmatrix} = \begin{bmatrix} \nabla V_1 \\ \nabla V_2 \\ \nabla V_3 \\ \vdots \\ \nabla V_n \end{bmatrix}$

This implies that $V(x) = \int_0^x (\nabla V)^T dx$

x can be interpreted into arbitrary points in the phase space that is $x_1, x_2, x_3, \ldots, x_n$

Note that $a_i's$ are positive, then from ∇V, we determine $V'(x)$ as $(\nabla V)^T x'$.

$$V'(x) = \begin{pmatrix}\begin{bmatrix} a_{11}x_1 + a_{12}x_2 \\ a_{21}x_1 + a_{22}x_2 \end{bmatrix}\end{pmatrix}^T \begin{bmatrix} Bw_0 + \varphi x_2 - (\gamma_3 + \mu_0)x_1 \\ B(1-w_0) + \gamma_3 x_1 - (\mu_0 + \varphi)x_2 \end{bmatrix}$$

$$= [a_{11}x_1 + a_{12}x_2 \quad a_{21}x_1 + a_{22}x_2] \begin{bmatrix} Bw_0 + \varphi x_2 - (\gamma_3 + \mu_0)x_1 \\ B(1-w_0) + \gamma_3 x_1 - (\mu_0 + \varphi)x_2 \end{bmatrix}$$

$$= \big((a_{12} - a_{22})x_2{}^2 + (a_{11} - a_{21})x_1x_2\big)\varphi + (-a_{22}x_2{}^2 + (-a_{21} - a_{12})x_1x_2 - a_{11}x_1{}^2)\mu_0 + \big((a_{22} - a_{12})x_1x_2 + (a_{21} - a_{11})x_1{}^2\big)\gamma_3 + \big((Ba_{12} - Ba_{22})w_0 + Ba_{22}\big)x_2 + ((Ba_{11} - Ba_{21})w_0 + Ba_{21})x_1$$

$$V'(x) = -x_2{}^2\mu_0 - 2x_1x_2\mu_0 - x_1{}^2\mu_0 + Bx_2 + Bx_1 \tag{13}$$

And in terms of the basic reproduction number, R_0 we have that

$$V'(x) = -(x_2{}^2 + 2x_1x_2 + x_1{}^2)\mu_0 + \left(\big((R_0 - 1)(x_1 + x_2)\big) + (x_1 + x_2)\ \frac{z\mu_0}{R_0^2 y}\right)$$

where $z = \ (x_1\beta(\mu_0 + \mu_1 + \alpha + \theta + \varepsilon q\gamma_1)$

and $y = \ (\gamma_2 + \mu_0 + \sigma)(\mu_0 + \gamma_1)(\mu_0 + \mu_1 + \alpha + \theta)$

For (x) , again from satisfying the curl requirement where we let $a_{11} = a_{12} = a_{21} = a_{22} = 1$,

$$V(x) = \int_0^{x_1, x_2 = 0} (x_1 + x_2)\, dx_1 + \int_0^{x_2, x_1 = 0} (x_1 + x_2)\, dx_2$$

$$= \frac{x_1^2}{2} + \frac{x_2^2}{2}$$

$$= \frac{1}{2}(x_1^2 + x_2^2)$$

And this implies that

$$V(x) = \frac{1}{2}(S_0^2 + V_0^2) > 0 \tag{14}$$

And

$$V'(x) = \ -\mu_0(S_0^2 + V_0^2) + \ [((R_0 - 1)(S_0 + V_0)] + (S_0 + V_0)\ \frac{z_0}{R_0 y_0}] \tag{15}$$

where $z_0 = \ S_0\beta\mu_0(\mu_1 + \mu_0 + \theta + q\gamma_1\varepsilon + \alpha)\sigma$ and

$y_0 = \ (\gamma_2 + \mu_0 + \sigma)(\mu_0 + \gamma_1)(\mu_0 + \mu_1 + \alpha + \theta)$

$V'(x)$ is negative definite if $R_0 < 1$, $and\ x_1 + x_2 > 0$

Hence the equilibrium state $f(0, t)$ is asymptotically stable.

Theorem 2 The disease-free equilibrium of the model system (3) is globally asymptotically stable if $R_0 < 1$

Proof

Having gotten from theorem that

$V(x) = \frac{1}{2}(S_0^2 + V_0^2) > 0$

and

$$V'(x) = \ -\mu_0(S_0^2 + V_0^2) + \ [((R_0 - 1)(S_0 + V_0)] + S_0 + V_0)\ \frac{z\mu_0}{R_0^2 y}]$$

Where $z = \ S_0\,\beta(\mu_0 + \mu_1 + \alpha + \theta + \varepsilon q\gamma_1)$ and

$y = \ (\gamma_2 + \mu_0 + \sigma)(\mu_0 + \gamma_1)(\mu_0 + \mu_1 + \alpha + \theta)$

Recall on disease-free equilibrium we have

$S' = Bw_0 + \varphi V_0 - (\mu_0 + \gamma_3)S_0 = 0$

$V' = B(1 - w_0) + \gamma_3 S_0 - (\mu_0 + \varphi)V_0 = 0$

If we let $S_0 = x_1, V_0 = x_2$, we will have that

$V(x) = \frac{1}{2}(x_1 + x_2)$ and

$V'(x) = B(x_1 + x_2) - \mu_0(x_1^2 + x_2^2)$

$$= -\mu_0(x_1^2 + x_2^2) + \ [((R_0 - 1)(x_1 + x_2)] + x_1 + x_2)\ \frac{z\mu_0}{R_0^2 y}]$$

Where $z = \ (x_1\beta(\mu_0 + \mu_1 + \alpha + \theta + \varepsilon q\gamma_1)$ and

$y = \ (\gamma_2 + \mu_0 + \sigma)(\mu_0 + \gamma_1)(\mu_0 + \mu_1 + \alpha + \theta)$

From $V(x) = \frac{1}{2}(x_1 + x_2)$

when $\|x_1\| \to \infty,\ V(x) \to \infty$

and when $\|x_2\| \to \infty,\ V(x) \to \infty$

This imply that $V(x)$ is radially unbounded, therefore since $V(x)$ is positive definite and radially unbounded and $V'(x)$ is negative definite if $R_0 < 1$. The model system (3) is globally asymptotically stable if $R_0 < 1$.

Theorem 3 If $R_0 > 1$, the endemic equilibrium point $D^* = [S^*, E^*, A^*, C^*, V^*, R^*]$ is locally asymptotically stable and if $R_0 < 1$, then the endemic equilibrium points of the model system (3) are unstable

Proof

We need to construct a Lyapunov function $V(x)$ which will be positive definite and $V'(x)$ that will be negative definite. Using Krasovskii method of constructing Lyapunov function.

We consider an autonomous system that is nonlinear

$$x' = f(x)$$

Where in our own case x is a six-dimensional vector, we assume that the equilibrium is 0 that is $f(0,t) = 0$. Now considering the model system (3), we have that

$$f = \begin{bmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \\ f_5 \\ f_6 \end{bmatrix}, \quad \text{and} \quad x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \end{bmatrix}$$

Also from the model system 3, we let $S' = f_1,\ E' = f_2,\ A' = f_3, C' = f_4,\ V' = f_5,\ R' = f_6$ and $S = x_1, E = x_2, A = x_3, C = x_4, V = x_5\ and\ R = x_6$

This implies that

$$\begin{aligned}
f_1 &= Bw_0 + \varphi x_5 - (\lambda + \gamma_3 + \mu_0)x_1 \\
f_2 &= \lambda x_1 - (\gamma_2 + \mu_0 + \sigma)x_2 \\
f_3 &= \sigma x_2 - (\mu_0 + \gamma_1)x_3 \\
f_4 &= q\gamma_1 x_3 - (\mu_0 + \mu_1 + \alpha + \theta)x_4 \\
f_5 &= B(1 - w_0) + \gamma_3 x_1 + \gamma_2 x_2 - (\mu_0 + \varphi)x_5 \\
f_6 &= (1 - q)\gamma_1 x_3 + (\alpha + \theta)x_4 - \mu_0 x_6
\end{aligned} \tag{16}$$

Where $\lambda = \frac{\beta(A + \varepsilon C)}{N}$

Then for our model system,

$$f(x) = \begin{pmatrix} Bw_0 + \varphi x_5 - (\lambda + \gamma_3 + \mu_0)x_1 \\ \lambda x_1 - (\gamma_2 + \mu_0 + \sigma)x_2 \\ \sigma x_2 - (\mu_0 + \gamma_1)x_3 \\ q\gamma_1 x_3 - (\mu_0 + \mu_1 + \alpha + \theta)x_4 \\ B(1 - w_0) + \gamma_3 x_1 + \gamma_2 x_2 - (\mu_0 + \varphi)x_5 \\ (1 - q)\gamma_1 x_3 + (\alpha + \theta)x_4 - \mu_0 x_6 \end{pmatrix} \tag{17}$$

Assume that $f(x)$ has continuous first partial derivative, according to Krasovskii method, we define

$V(x) = f^T(x)f(x), V'(x) = (f')^T(x)f(x) + f^T(x)f'(x)$ and $f'(x) = \frac{\partial f}{\partial x}\frac{\partial x}{\partial t} = A(x)f(x)$

Therefore

$$V'(x) = [A(x)f(x)]^T f(x) + f^T(x)A(x)f(x)$$

$$V'(x) = f^T(x)[A^T(x) + A(x)\ ]f(x)$$

Since $f'(x) = \frac{\partial f}{\partial x}\frac{\partial x}{\partial t} = A(x)f(x)$, this implies that $A(x) = \frac{\partial f}{\partial x}$ is the jacobian matrix of the model.

$$\boldsymbol{A(x)} = \begin{pmatrix} -\mu_0 - \lambda - \gamma_3 & 0 & -\frac{x_1\beta}{N} & -\frac{x_1\beta\varepsilon}{N} & \varphi & 0 \\ \lambda & -\sigma - \mu_0 - \gamma_2 & 0 & 0 & 0 & 0 \\ 0 & \sigma & -\mu_0 - \gamma_1 & 0 & 0 & 0 \\ 0 & 0 & q\gamma_1 & -\mu_1 - \mu_0 - \theta - \alpha & 0 & 0 \\ \gamma_3 & \gamma_2 & 0 & 0 & -\varphi - \mu_0 & 0 \\ 0 & 0 & (1 - q)\gamma_1 & \theta + \alpha & 0 & -\mu_0 \end{pmatrix} \tag{18}$$

Let's define a function $\hat{F} = A(x) + A^T(x)$, where $A^T(x)$ is the transpose of $A(x)$, that is

$$A^T(x) = \begin{pmatrix} -\mu_0-\lambda-\gamma_3 & \lambda & 0 & 0 & \gamma_3 & 0 \\ 0 & -\sigma-\mu_0-\gamma_2 & \sigma & 0 & \gamma_2 & 0 \\ -\frac{x_1\beta}{N} & 0 & -\mu_0-\gamma_1 & q\gamma_1 & 0 & (1-q)\gamma_1 \\ -\frac{x_1\beta\varepsilon}{N} & 0 & 0 & -\mu_1-\mu_0-\theta-\alpha & 0 & \theta+\alpha \\ \varphi & 0 & 0 & 0 & -\varphi-\mu_0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu_0 \end{pmatrix} \quad (19)$$

Then $\hat{F} = A(x) + A^T(x)$ becomes

$$\begin{pmatrix} -2\mu_0-2\lambda-2\gamma_3 & \lambda & -\frac{x_1\beta}{N} & -\frac{x_1\beta\varepsilon}{N} & \varphi+\gamma_3 & 0 \\ \lambda & -2\sigma-2\mu_0-2\gamma_2 & \sigma & 0 & \gamma_2 & 0 \\ -\frac{x_1\beta}{N} & \sigma & -2\mu_0-2\gamma_1 & q\gamma_1 & 0 & (1-q)\gamma_1 \\ -\frac{x_1\beta\varepsilon}{N} & 0 & q\gamma_1 & -2\mu_1-2\mu_0-2\theta-2\alpha & 0 & \theta+\alpha \\ \varphi+\gamma_3 & \gamma_2 & 0 & 0 & -2\varphi-2\mu_0 & 0 \\ 0 & 0 & (1-q)\gamma_1 & \theta+\alpha & 0 & -2\mu_0 \end{pmatrix} \quad (20)$$

Recall that

$V'(x) = f^T(x)[A^T(x) + A(x)\ ]f(x)$

And where $\hat{F} = A(x) + A^T$, then $V'(x) = f^T(x)\hat{F}\,f(x)$

According to the Krasovaskii method, from the expression

$V'(x) = f^T(x)\hat{F}\,f(x)$, $V'(x)$ is negative definite if we have that $-\widehat{F_1} = -[A(x) + A^T]$, and $\widehat{F_1}$ is positive definite. So, we have that $-\widehat{F_1} = -[A(x) + A^T]$ *becomes*

$$\begin{pmatrix} 2\mu_0+2\lambda+2\gamma_3 & -\lambda & \frac{x_1\beta}{N} & \frac{x_1\beta\varepsilon}{N} & -(\varphi+\gamma_3) & 0 \\ -\lambda & 2\sigma+2\mu_0+2\gamma_2 & \sigma- & 0 & -\gamma_2 & 0 \\ \frac{x_1\beta}{N} & -\sigma & 2\mu_0+2\gamma_1 & -q\gamma_1 & 0 & -(1-q)\gamma_1 \\ \frac{x_1\beta\varepsilon}{N} & 0 & -q\gamma_1 & 2\mu_1+2\mu_0+2\theta+2\alpha & 0 & -(\theta+\alpha) \\ -(\varphi+\gamma_{3)} & -\gamma_2 & 0 & 0 & 2\varphi+2\mu_0 & 0 \\ 0 & 0 & -(1-q)\gamma_1 & -(\theta+\alpha) & 0 & 2\mu_0 \end{pmatrix}$$

To check the definiteness of $\widehat{F_1}$, using the leading principal submatrices. From the system of equations, $n = 6$ and $k = 1,2,\ldots,5$. And find the determinant of the leading principal minors of $\widehat{F_1}$, thus $D_1\, is\, 2\mu_0 > 0$, The determinant of $D_2\, is\, 2((\varphi+\mu_0)\mu_0) > 0$, The determinant of D_3 , $|D_3| = (2\mu_1+2\mu_0+2\theta+2\alpha)\left(2\left((\varphi+\mu_0)\mu_0\right)\right) + ((\theta+\alpha)^2 2(\varphi+\mu_0)) > 0$,

The determinant of D_4 , $|D_4| = (2\mu_0+2\gamma_1)(2\mu_1+2\mu_0+2\theta+2\alpha)(|D_2|) + (|D_2|)(q\gamma_1)^2$

The determinant of D_5 , $|D_5| = (2\sigma+2\mu_0+2\gamma_2)\left((|D_2|)\left((2\mu_0+2\gamma_1)(2\mu_1+2\mu_0+2\theta+2\alpha)+(q\gamma_1)^2\right)\right) > \mathbf{0}$

And the determinant of D_6 ,

$|D_6| = (R_0-1)\left(4\mu_0(\mu_0+\lambda+\gamma_3)\left((x_1\beta\mu_1+x_1\beta\mu_0+x_1\beta\theta+x_1\alpha\beta)\sigma+q\gamma_1\varepsilon\right)(\varphi+\mu_0)\right)(NR_0)^{-1}$- $\boldsymbol{\lambda^2}\left(\left(2\left((\varphi+\mu_0)\mu_0\right)\right)\left((2\mu_0+2\gamma_1)(2\mu_1+2\mu_0+2\theta+2\alpha)+(q\gamma_1)^2\right)\right)$

$-\left(\left(4\mu_0(\mu_0+\lambda+\gamma_3)\left((x_1\beta\mu_1+x_1\beta\mu_0+x_1\beta\theta+x_1\alpha\beta)\sigma+q\gamma_1\varepsilon\right)(\varphi+\mu_0)\right)(N)^{-1}\right)$

Since all the determinant of leading principal minors of $\widehat{F_1}$ are positive if $R_0 > 1$ and if the inequality

$$\left(4\mu_0(\mu_0+\lambda+\gamma_3)\left((x_1\beta\mu_1+x_1\beta\mu_0+x_1\beta\theta+x_1\alpha\beta)\sigma+q\gamma_1\varepsilon\right)(\varphi+\mu_0)\right)(NR_0)^{-1} >$$

$$\boldsymbol{\lambda^2}\left(\left(2\left((\varphi+\mu_0)\mu_0\right)\right)\left((2\mu_0+2\gamma_1)(2\mu_1+2\mu_0+2\theta+2\alpha)+(q\gamma_1)^2\right)\right)$$

$$-\left(\left(4\mu_0(\mu_0+\lambda+\gamma_3)\left((x_1\beta\mu_1+x_1\beta\mu_0+x_1\beta\theta+x_1\alpha\beta)\sigma+q\gamma_1\varepsilon\right)(\varphi+\mu_0)\right)(N)^{-1}\right)$$

Is true, then $\widehat{F_1}$ is positive definite

Therefore, if $R_0 > 1$, $\widehat{F_1}$ is positive definite which imply that the derivative of $V(x)$ that is $V'(x)$ is negative definite

Then

$V(x) = (Bw_0 + \varphi x_5 - (\lambda+\gamma_3+\mu_0)x_1)^2 + (\lambda x_1 - (\gamma_2+\mu_0+\sigma)x_2)^2 + (\sigma x_2 - (\mu_0+\gamma_1)x_3)^2 + (q\gamma_1 x_3 - (\mu_0+\mu_1+\alpha+\theta)x_4)^2 + (B(1-w_0) + \gamma_3 x_1 + \gamma_2 x_2 - (\mu_0+\varphi)x_5)^2 + ((1-q)\gamma_1 x_3 + (\alpha+\theta)x_4 - \mu_0 x_6)^2$

Clearly, $V(x) > 0$ which imply that $V(x)$ is positive definite and since $-\widehat{F_1}$ is positive definite if $R_0 > 1$ which imply that the derivative of $V(x)$ that is $V'(x)$ is negative definite according to krasvoskii method. Hence the endemic equilibrium is locally asymptotically stable if $R_0 > 1$.

Theorem 4.4 If $R_0 > 1$, the endemic equilibrium point is globally asymptotically stable

Proof

Since the study have constructed the Lyapunov function of the endemic equilibrium point of the model and its derivative using krasvoskii method;

Clearly, $V(x)$ is positive definite and

$V'(x) = f^T(x)\hat{F}\, f(x)$ and having $\hat{F_1} = -[A(x) + A^T] = -\hat{F}$, is negative definite. Since $-\hat{F}$ is positive definite if $R_0 > 1$, and V(x) is radially unbounded since as norm of x tends to infinity, the $V(x)$ also tends to infinity.

That is;

$$||x|| \underset{x\to\infty}{\longrightarrow} \infty \implies V(x) \underset{x\to\infty}{\longrightarrow} \infty$$

Hence the endemic equilibrium point of model is globally asymptotically stable.

4. Numerical Simulation for Stability Analysis

Taking the values of the parameter from the Table below

Parameters	Interpretation	Estimate
B	Recruitment	0.09121
μ_0	Natural mortality	0.09121
μ_1	HBV-related mortality	0.041
ω_0	Proportion of non-vaccinated recruitment	0.3
σ	Rate of moving from exposed to acute state	0.36
γ_2	Post exposed vaccinated of the exposed individuals	0.45
φ	vaccination waning rate	0.53
β	Transmission coefficient	0.655
ε	Reduced transmission rate relative to acute infection by carriers	0.5
γ_1	Rate of moving from acute to other compartments	0.44
q	Rate of moving from acute to carrier	0.5
α	Rate of moving from carrier to immune by treatment	0.6
θ	Rate of moving from carrier to immune naturally	0.6
γ_3	Rate of susceptible get vaccinated	0.5

Table 4.3: Parameter values for the model system 3.3 at $R_0 < 1$ for the Numerical simulation of model system 3.3 without delay

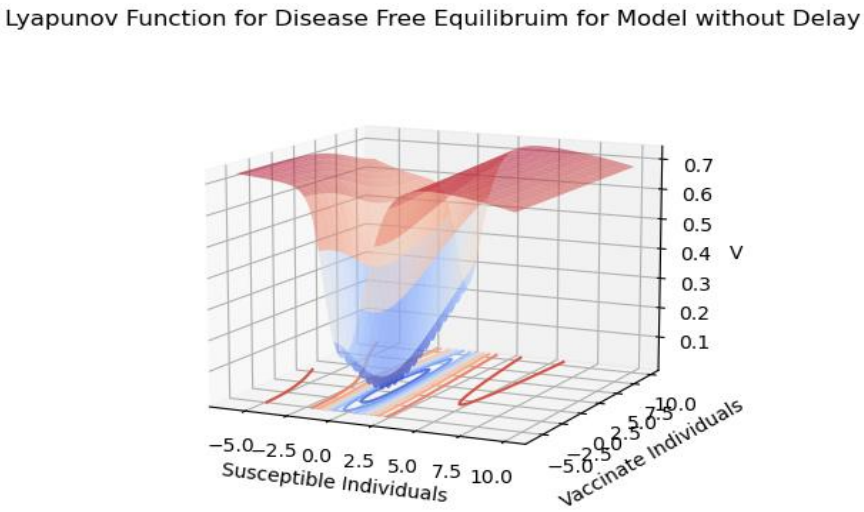

Figure 11: Numerical Simulation of the lyapunov funtion for Disease free equilibruim at $R_0 < 1$. It is observed that the Lyapunov function of the diseases free equilibrium is positive except at zero.

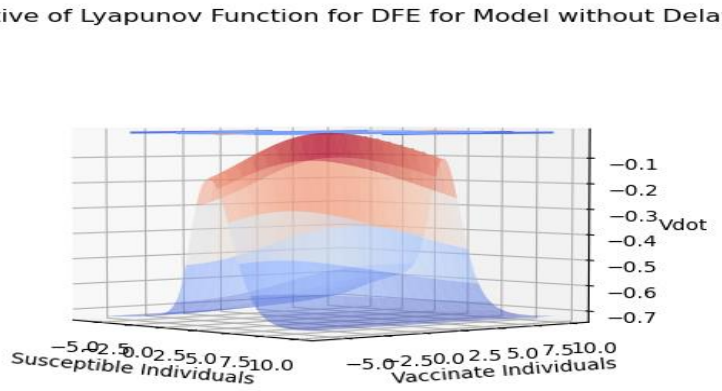

Figure 2: Numerical Simulation of the Derivative of Lyapunov function for Disease free equilibrium at $R_0 < 1$. This shows that the derivative of the Lyapunov function is negative everywhere except at zero.

4. Conclusion

The paper focused on the stability of the model of HBV dynamics which incorporates vaccination, treatment and post-exposure prophylaxis. The study established the disease-free equilibrium and the endemic equilibrium, and showed that the disease-free equilibrium is local and global asymptotically stable as $R_0 < 1$. Also, the endemic equilibrium is local and global asymptotically stable as $R_0 > 1$ Our analysis and the numerical simulation shown in Figure 1 and Figure 2 that the Lyapunov function of the disease-free equilibrium is positive definite and the derivative of the Lyapunov function is negative definite. Hence, this implies that the disease-free equilibrium is stable when the basic reproduction number is less than one. The study suggests that the use of post-exposure prophylaxis or combining the post-exposure prophylaxis with vaccination (both the vaccination of infants) and treatment will keep the basic reproduction number less than one.

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