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On the dynamics of hepatitis B virus disease

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Abstract

Hepatitis B is a serious liver infection caused by hepatitis B virus (HBV). In this paper, we review the deterministic model of HBV proposed by Emerenini and Inyama in 2018 to carry out a rigorous mathematical analysis. The analysis of the model reveals that an endemic equilibrium exists in addition to the disease free equilibrium (DFE) point. The vaccinated reproduction number, $\mathcal{R}_v$ is derived and revealed that if $\mathcal{R}_v < 1$, the DFE is locally asymptotically stable and is unstable when $\mathcal{R}_v > 1$, while the endemic equilibrium point (EEP) is the only asymptotic stable equilibrium point when $\mathcal{R}_v > 1$. The global asymptotic stability of both the disease free equilibrium and endemic equilibrium points are proved using Lyapunov function in conjunction with LaSalles' Invariance Principle. Furthermore, we obtain the minimum value of the fraction of newborn babies required to be vaccinated for effective disease control.

1. Introduction

Hepatitis B virus (HBV) is a potentially life threatening liver infection which is a DNA virus classified in the virus family of Hepadnaviridae [16]. It is a globally infectious disease that can lead to acute or chronic conditions. Although there

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is a vaccine that offers protection against the virus, current treatments which prevent the virus from replicating are not curative for infected individuals [19]. HBV is easily contracted from a victim through contact of body fluids, either through sexual contact, blood contact or even saliva, breast feeding, and mother to child transmission. It could also be contracted if by chance a person consumes the waste passed out from a carrier. Slight contact with these fluids can transmit the disease. If not treated with caution, the hepatitis virus would gradually grow in to a more severe state which is known as the Hepatitis B [2, 24]. Some existing literatures have confirmed many of the aforementioned routes of transmission and reported that the rate of HBV prevalence increases with age. Various studies reveal that direct contact with blood is an important mode of HBV transmissions [5, 16]. A vaccine against HB has been available since 1982, nevertheless there is still an increase in its transmission and spread. It was revealed that HBV can survive outside the human body for at least 7 days and during this period HBV can still cause infection if it enters any unimmunized human body [23].

Most HB carriers are asymptomatic during the acute infection phase, while some people experience acute illness with symptoms that last several weeks, including yellowing of the skin and eyes (jaundice), dark urine, extreme fatigue, nausea, vomiting and abdominal pain. A few of persons with acute hepatitis can develop acute liver failure, which can lead to death. The hepatitis B virus can also cause a chronic liver infection that can later develop into cirrhosis (a scarring of the liver) or liver cancer [23]. Hepatitis B virus becomes a public health problem worldwide since it infects over two billion people with high prevalence in the developing countries [16, 23]. It was reported that 280 million of them are chronic carriers from whom about 2 million die each year as a result of cirrhosis or primary liver cell cancer induced by the virus [5]. The HBV results in 80% of primary liver cancer cases, which is one of the leading causes of death in Asia and Africa [3]. Clement *et al.* reported in [3], that infected adults who become chronic carriers ranges from 5% to 10% and the remaining eliminates the virus from their body without sequence. In deed, about one forth of chronic carriers die due to hepatitis complications of chronic infection, some remain lifelong carriers while others will clear the infection after varying intervals [27]. A region of high endemicity like Sub-Sahara Africa has an average carriers rate ranging between 10% to 20% in its general population [23]. In addition, 70% to 95% of adults in such a region have at least one marker of HBV [11]. In a similar note, it has been estimated that 40% of West African children will be infected by age two years and over 7% in a population is classified as hyper endemic [11]. The recorded HBV carriage rate in Nigeria ranges between 9% to 39% [5, 20, 23].

In 2000, Alfonseca *et al.* [1] proposed simulation mathematical models for two different epidemic situations viz: Hepatitis B in a cohort of newborns followed for life, and one of the danger groups in the current AIDS epidemic. Their study described the rationale behind the deterministic modelling of both situations, and the way to test alternative policies, such as vaccination, preventive measures, or the effects of new drugs on AIDs. The dynamics of a delay model of hepatitis B virus infection with logistic hepatocyte growth was presented in [4]. In addition to the results of some existing models in the literature with constant hepatocyte growth of convergence to a virus free or a chronic steady state, their model admits sustained oscillations. The analysis reveals that stability of this chronic steady state is dependent on both the rate of hepatocyte regeneration and the virulence of the disease. Interestingly, numerical simulations of the model show the existence of an attracting periodic orbit when the chronic steady state is unstable. Moreover, the hepatocyte populations are very small in the periodic orbit, and such a state likely represents acute liver failure.

A model for the transmission dynamics of hepatitis B in Xinjiang, China was presented in [25], incorporating exponential birth rate and vertical transmission. The modified reproductive number is obtained which determine the disease spread. In fact, the numerical simulation of the model reveals that the cumulative new cases of HBV could attain about 600,000 cases without stronger or more effective control measures by the end of 2017. Furthermore, sensitivity analysis showed that enhancing the vaccination rate for newborns in Xinjiang is very effective measure of containing the transmission of HBV. Hepatitis B optimal control model with vertical transmission was proposed by Nana-Kyere *et al.* [13], to investigate the cost effective control efforts in reducing the number of exposed and infective. The numerical simulation of the model revealed that the number of exposed and infected humans decreased in the optimality system. Also, the control analysis indicates that the optimal control strategies have an incomparable effect for the reduction of the infected individuals as compared to the model without control. Moreover, the simulation results showed that despite the vertical transmission incidence, the proposed control strategy is effective in the reduction of the number of the infective. A mathematical model of HBV with differential infectivity and two types of transmissions was proposed in [10]. The analysis of the model reveals the highest risk factors for the spread of HBV in the community.

Pang and Ciu, [15] proposed a model of hepatitis B virus with vaccination to describe the dynamics of HBV transmission. The model can be used for predicting the long-term effectiveness of the immunization programme and help in selecting optimal strategies for nationwide HBV vaccination. In another development, a simulation model was proposed for global control and eradication of HBV infection [14]. This study indicated that vaccination of infants and neonates decreased new infections and averted millions new chronic infections by 2015 and will have

prevented at least a million deaths by 2030. Moreover, the model analysis also revealed that without scale-up of existing interventions, millions cumulative new cases of chronic HBV infection and HBV-related mortality will be recorded between 2015 and 2030 due to ongoing transmission in some regions and poor access to treatment for infected individuals. They also reported that incidence of new chronic infections elimination threshold could be reached by the year 2090 worldwide and the annual cost could be peaked at US$7.5 billion globally, but decline rapidly. In addition to that, a deterministic compartmental model to explore the dynamics of acute and chronic HBV transmission and develop an optimal control strategy to contain the spread of the virus in a community was presented in [9]. The model analysis shows that HBV could be control by isolation of infected from non-infected individuals, treatment and vaccination to minimize the number of acute infected, chronically infected with hepatitis B individuals and maximize the number of susceptible and recovered individuals.

In a similar note, Emerenini and Inyama [6], presented a deterministic mathematical model for the dynamics of HBV transmission with vaccination of newborn babies and the treatment of infected individuals in controlling the disease. In their analysis only existence and local asymptotic stability of disease free equilibrium were presented. As the detailed mathematical analysis of the model was not carried out in [6], we here carry out such an analysis of the model to assess the impact of vaccination. In fact, we derive the threshold parameter which determines the persistence or otherwise of the HBV in a population. We also show that the model exhibits a unique endemic equilibrium point and prove the local and global asymptotic stabilities of both disease free and endemic equilibrium points.

The remaining part of the paper is organized as follows: In Section 2, the model description is provided, the model equilibria are determined and stability analysis is carried out in Section 3. In Section 4, the impact of vaccination is discussed. We then provide a concluding remark in Section 5.

2. Model description

This study reviews the deterministic model of HBV infection presented in [6] in order to carry out more rigorous mathematical analysis. we divide the total population at time t, denoted by $N(t)$ into five disjoint epidemiological classes which are Immunized individuals (M), susceptible individuals (S), latently exposed individuals (L), infectious individuals (I), and recovered individuals (R). Then the respective rate of transfer between these classes is as depicted in Figure 1 and as in [6] the required model is given in equation (1) below.

$$\begin{aligned}
\frac{dM}{dt} &= cP - (\phi + \mu)M, \\
\frac{dS}{dt} &= (1-c)P + \phi M + \pi R - \beta IS - \mu S, \\
\frac{dL}{dt} &= \beta IS - (q + k + \mu)L, \\
\frac{dI}{dt} &= kL - (\gamma + \tau + \mu)I, \\
\frac{dR}{dt} &= \gamma I + qL - (\pi + \mu)R,
\end{aligned} \tag{1}$$

with $N = M + S + L + I + R$.

In system (1), cP is the immunized newborn babies, ϕ is the rate of expiration of vaccine efficacy, μ is the natural death rate, π is the rate of transfer from recovered class to susceptible compartment, β is the effective contact rate, k is the progression rate from the latent class to the infectious class, γ is the recovery rate due to treatment of infectious individuals, q is the transfer rate from latent compartment to the recovered class, τ is the HBV induced mortality rate, and P population of newborn babies.
It follows from (1) that the equation of the total population is

$$\frac{dN}{dt} = P - \mu N(t) - \tau I. \tag{2}$$

Considering the trivial existence and uniqueness of local solution of (1) and following [21], we can present the basic properties of (1) below.

Lemma 2.1. *The solution of model (1) with positive initial conditions exist* $\forall t \geq 0$ *and is unique. Moreover,* $M(t) \geq 0, S(t) \geq 0, L(t) \geq 0, I(t) \geq 0$ *and* $R(t) \geq 0, \forall t \geq 0$.

Then, applying Lemma (2.1) on equation (2), we have the following result.

Lemma 2.2. *The closed region*

$$\mathcal{D} = \left\{ (M(t), S(t), L(t), I(t), R(t)) \in \mathbb{R}^5_+ : M(t) + S(t) + L(t) + I(t) + R(t) \leq \frac{P}{\mu} \right\}$$

of model (1) *is positively invariant and attracting.*

Proof. Equation (2), implies that

$$\frac{dN}{dt} \leq P - \mu N(t),$$

so that $\frac{dN}{dt} \leq 0$ when $N(t) > \frac{P}{\mu}$. Then, using a standard comparison theorem, we obtain

$$N(t) \leq N(0)e^{-\mu t} + \frac{P}{\mu}(1 - e^{-\mu t}).$$

Thus, $N(t) \leq \frac{P}{\mu}$ when $N(0) \leq \frac{P}{\mu}$ and so, $\mathcal{D}$ is positively invariant. Therefore, if $N(t) > \frac{P}{\mu}$, then either the solution enters $\mathcal{D}$ in finite time or $N(t)$ approaches $\frac{P}{\mu}$ and the infected state variables $L(t)$ and $I(t)$ go to zero. Hence $\mathcal{D}$ is attracting (i.e., all solutions in $\mathbb{R}^5_+$ eventually enter $\mathcal{D}$). □

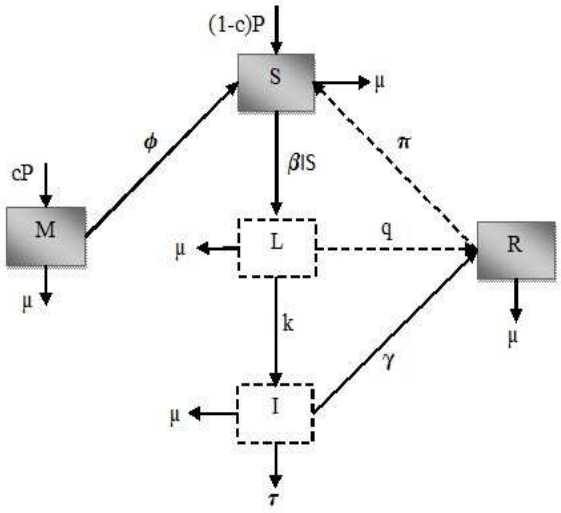

Figure 1: Schematic diagram of model (1)

3. Model equilibria and stability results

Let $E(M, S, L, I, R)$ be an equilibrium point of the system described in (1). Then at such a point the vector field of (1) is zero. In the absence of the disease there exist no trivial equilibrium since newborn babies are recruit as susceptible individuals and so, the population cannot be extinct. Therefore, a disease free equilibrium (DFE) exists and is presented as follows

$$E_0(M_0, S_0, L_0, I_0, R_0) = \left(\frac{cP}{\phi + \mu}, \frac{P[\phi + \mu(1-c)]}{\mu(\phi + \mu)}, 0, 0, 0 \right).$$

A threshold parameter called the basic reproduction number is required to establish the condition for linear stability of equilibria for disease transmission models, usually denoted by $\mathcal{R}_0$. In this case, the associated threshold parameter is represented by $\mathcal{R}_v$ due to vaccination [7]. Using the method and notation presented in [22], we denote the matrices for the new infection terms and that for the transition terms by F and V, respectively.

$$F = \begin{bmatrix} 0 & \beta S_0 \\ 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} q + k + \mu & 0 \\ -k & \gamma + \tau + \mu \end{bmatrix}.$$

Thus,

$$\begin{aligned} \mathcal{R}_v &= \varrho\left(FV^{-1}\right) = \frac{\beta k S_0}{(q + k + \mu)(\gamma + \tau + \mu)} \\ &= \frac{\beta k P[\phi + \mu(1-c)]}{\mu(\phi + \mu)(q + k + \mu)(\gamma + \tau + \mu)} \end{aligned} \tag{3}$$

It is worthy of notice that if $c = \phi = 0$, then (3) becomes the basic reproduction number

$$\mathcal{R}_0 = \frac{\beta k P}{\mu(q + k + \mu)(\gamma + \tau + \mu)} \tag{4}$$

Theorem 3.1. *The equilibrium point, E_0, of system (1) is locally asymptotically stable on $\mathcal{D}$ if $\mathcal{R}_v < 1$ and is unstable whenever $\mathcal{R}_v > 1$.*

Proof. The Jacobian matrix evaluated at E_0, denoted by J_0 is

$$J_0 = \begin{pmatrix} -Q_1 & 0 & 0 & 0 & 0 \\ \phi & -\mu & 0 & -\beta S_0 & \pi \\ 0 & 0 & -Q_2 & \beta S_0 & 0 \\ 0 & 0 & k & -Q_3 & 0 \\ 0 & 0 & q & \gamma & -Q_4 \end{pmatrix}, \tag{5}$$

with $Q_1 = \phi + \mu, Q_2 = q + k + \mu, Q_3 = \gamma + \tau + \mu$ and $Q_4 = \pi + \mu$. Then, the eigenvalues of this matrix are $-Q_1, -\mu, -Q_4$ and the eigenvalues of the submatrix J_0^* of J_0. The matrix J_0^* is obtained by deleting the first row and the first

column, the second row and second column and the last row and the last column of J_0. That is

$$J_0^* = \begin{pmatrix} -Q_2 & \beta S_0 \\ k & -Q_3 \end{pmatrix}.$$

Then the trace and determinant of J_0^* are respectively, given by

$$tr(J_0^*) = -(Q_2 + Q_3) < 0$$

and

$$\det(J_0^*) = Q_2Q_3 - k\beta S_0 = Q_2Q_3(1 - \mathcal{R}_v) > 0$$

if $\mathcal{R}_v < 1$. It follows that the eigenvalues of J_0^* have negative real parts. Hence the five eigenvalues of J_0 have negative real parts and so, the DFE, E_0 of model (1) is locally asymptotically stable when $\mathcal{R}_v < 1$. □

This theorem has an epidemiological implication that the disease (hepatitis B) cannot persist in the population if the infected subpopulations are in the basin of attraction of the equilibrium point E_0 whenever $\mathcal{R}_v < 1$.

3.1. **Endemic equilibrium point, EEP.** This is a point where HBV infectious individuals persist in the population. Therefore, at this point the vector field of (1) is equal to zero and so, the equilibrium point is the following

$$E^* = (S^*, E^*, I^*, F^*, L^*, A^*, R^*)$$

with

$$\begin{aligned} M^* &= \frac{cP}{Q_1}, \\ S^* &= \frac{Q_2Q_3}{\beta k}, \\ L^* &= \frac{\mu Q_3 \prod_{i=1}^{4} Q_i(\mathcal{R}_v - 1)}{\beta Q_1 k\{\mu[qQ_3 + \gamma(k + Q_4)] + Q_4(\mu + \tau)(k + \mu)\}}, \\ I^* &= \frac{\mu \prod_{i=1}^{4} Q_i(\mathcal{R}_v - 1)}{\beta Q_1\{\mu[qQ_3 + \gamma(k + Q_4)] + Q_4(\mu + \tau)(k + \mu)\}}, \\ R^* &= \frac{\mu(\gamma k + qQ_3) \prod_{i=1}^{3} Q_i(\mathcal{R}_v - 1)}{\beta Q_1 k\{\mu[qQ_3 + \gamma(k + Q_4)] + Q_4(\mu + \tau)(k + \mu)\}}. \end{aligned} \tag{6}$$

We can prove the local stability of E^* by showing the existence of a transcritical bifurcation between E_0 and E^*. That is to show there is an exchange of stability

between E_0 and E^* at $\mathcal{R}_v = 1$ or equivalently $\beta^* = \frac{\mu(\phi+\mu)(q+k+\mu)(\gamma+\tau+\mu)}{kP[\phi+\mu(1-c)]}$. This is presented in the following theorem.

Theorem 3.2. *Model (1) exhibits a transcritical bifurcation at E_0 if the bifurcation parameter $\beta^* = \frac{\mu(\phi+\mu)(q+k+\mu)(\gamma+\tau+\mu)}{kP[\phi+\mu(1-c)]}$ or equivalently $\mathcal{R}_v = 1$.*

Proof. We denote by f the vector field of system (1) to obtain

$$f(M,S,L,I,R;\beta) = \begin{pmatrix} cP-(\phi+\mu)M \\ (1-c)P+\phi M+\pi R-\beta IS-\mu S \\ \beta IS-(q+k+\mu)L \\ kL-(\gamma+\tau+\mu)I \\ \gamma I+qL-(\pi+\mu)R \end{pmatrix}. \tag{7}$$

The Jacobian matrix evaluated at E_0, denoted by J_0 as presented in (5) is given by

$$J_0 = \begin{pmatrix} -Q_1 & 0 & 0 & 0 & 0 \\ \phi & -\mu & 0 & -\beta S_0 & \pi \\ 0 & 0 & -Q_2 & \beta S_0 & 0 \\ 0 & 0 & k & -Q_3 & 0 \\ 0 & 0 & q & \gamma & -Q_4 \end{pmatrix},$$

This matrix has the determinant

$$\det J_0 = \prod_{i=1}^{4} Q_i \mu(\mathcal{R}_v - 1),$$

which is zero if $\mathcal{R}_v = 1$ and the trace

$$\mathrm{tr} J_0 = -\left(\mu + \sum_{i=1}^{4} Q_i\right) \neq 0.$$

It follows that, J_0 has a simple zero eigenvalue and so, we can apply Sotomayor theorem to establish the existence of transcritical bifurcation at E_0 [17]. For the conditions of this phenomenon, let an eigenvector of the matrix J_0 corresponding to the eigenvalue $\lambda = 0$ be $U = (u_1, u_2, u_3, u_4, u_5)^T$. Then we compute this vector, using the standard computation of an eigenvector as follows:

$$U = \begin{pmatrix} 0 & \frac{\prod_{i=1}^{4} Q_i \mathcal{R}_0 - Q_1(k\gamma - Q_3)}{k\mu Q_1 Q_2} & \frac{Q_3}{k} & 1 & \frac{k\gamma+Q_3}{kQ_4} \end{pmatrix}^T. \tag{8}$$

Now, let $V = (v_1, v_2, v_3, v_4, v_5)^T$ be an eigenvector of the transpose of the Jacobian matrix J_0. The eigenvector V corresponding to the eigenvalue $\lambda = 0$ is then given by

$$V = \begin{pmatrix} 0 & 0 & \frac{kQ_4+q\gamma}{Q_2Q_4} & 1 & \frac{\gamma}{Q_4} \end{pmatrix}^T.$$

The derivative of the vector field $f(M,S,L,I,R;\beta)$ in (7) with respect to the bifurcation parameter β at the equilibrium point E_0 is

$$f_\beta(E_0;\beta) = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \end{pmatrix}^T$$

and so,

$$V^T f_\beta(E_0;\beta) = \begin{pmatrix} 0 & 0 & \frac{kQ_4+q\gamma}{Q_2Q_4} & 1 & \frac{\gamma}{Q_4} \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = 0. \tag{9}$$

The expression $Df_\beta(M,S,L,I,R;\beta)U$ as defined in [17] is

$$Df_\beta(M,S,L,I,R;\beta)U = \frac{\partial f_\beta}{\partial M}u_1 + \frac{\partial f_\beta}{\partial S}u_2 + \frac{\partial f_\beta}{\partial L}u_3 + \frac{\partial f_\beta}{\partial I}u_4 + \frac{\partial f_\beta}{\partial R}u_5.$$

Evaluating this expression at E_0 and using (8) gives

$$Df_\beta(E_0;\beta)U = \begin{pmatrix} 0 \\ \frac{\prod_{i=1}^4 Q_i\mathcal{R}_0 - Q_1(k\gamma - Q_3)}{k\mu Q_1 Q_2} \\ \frac{Q_3}{k} \\ 1 \\ \frac{k\gamma+Q_3}{kQ_4} \end{pmatrix}.$$

Thus,

$$V^T[Df_\beta(E_0;\beta)] = \begin{pmatrix} 0 & 0 & \frac{kQ_4+q\gamma}{Q_2Q_4} & 1 & \frac{\gamma}{Q_4} \end{pmatrix} \begin{pmatrix} 0 \\ \frac{\prod_{i=1}^4 Q_i\mathcal{R}_0 - Q_1(k\gamma - Q_3)}{k\mu Q_1 Q_2} \\ \frac{Q_3}{k} \\ 1 \\ \frac{k\gamma+Q_3}{kQ_4} \end{pmatrix} \tag{10}$$

$$= \frac{Q_3(kQ_4+q\gamma) + Q_4\gamma(k\gamma+Q_3) + kQ_2Q_4^2}{kQ_2Q_4^2} \neq 0.$$

Also $D^2f(x;\beta)(U,U)$ is defined in [17] as follows:

$$D^2f(x;\beta)(U,U) = \sum_{k,i,j=1}^{5} \frac{\partial^2 f_k}{\partial x_i \partial x_j} u_i u_j.$$

Expanding and evaluating this using (8) at the point E_0, we obtain

$$D^2 f(E_0;\beta)(U,U) = \begin{pmatrix} 0 \\ 0 \\ \frac{\beta Q_3}{k} \\ 0 \\ 0 \end{pmatrix}.$$

Hence,

$$V^T[D^2 f(E_0;\beta)(U,U)] = \begin{pmatrix} 0 & 0 & \frac{kQ_4+q\gamma}{Q_2Q_4} & 1 & \frac{\gamma}{Q_4} \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ \frac{\beta Q_3}{k} \\ 0 \\ 0 \end{pmatrix} \tag{11}$$

$$= \frac{\beta Q_3[kQ_4 + q\gamma]}{kQ_2Q_4} \neq 0.$$

The proof follows from conditions (9), (10) and (11) by Sotomayor theorem [17]. ■ □

Theorem 3.2 asserts that when $\mathcal{R}_v < 1$ or equivalently $\beta = \beta^* = \frac{\mu(\phi+\mu)(q+k+\mu)(\gamma+\tau+\mu)}{kP[\phi+\mu(1-c)]}$, the only locally asymptotic stable equilibrium point is the disease free equilibrium E^0. If $\mathcal{R}_v > 1$ (i.e., $\beta > \beta^*$), then E_0 losses stability so that the unique endemic equilibrium E^* becomes locally asymptotically stable. Indeed, if $\mathcal{R}_v < 1$ the hepatitis B cannot invade the population if the infectious subpopulations are in the basin of attraction of E_0. While there is an endemic persistence when $\mathcal{R}_v > 1$.

3.2. **Global stability result of the DFE.** Considering the local asymptotic stability result of the DFE, E_0 as presented in Theorem 2, we prove in the following theorem its global stability.

Theorem 3.3. *The equilibrium point E_0 of system (1) is globally asymptotically stable on $\mathcal{D}$ when $\mathcal{R}_v \leq 1$.*

Proof. We define the following Lyapunov function

$$\Phi = kL + (q + k + \mu)I.$$

Then, the derivative of this function with respect to time along the solutions of (1) is

$$\begin{aligned}\dot{\Phi} &= k\dot{L} + (q+k+\mu)\dot{I}\\ &= k[\beta IS - (q+k+\mu)L] + (q+k+\mu)[kL - (\gamma+\tau+\mu)I],\\ &= [k\beta S - (q+k+\mu)(\gamma+\tau+\mu)]I,\\ &\leq [k\beta S_0 - (q+k+\mu)(\gamma+\tau+\mu)]I,\\ &= -(q+k+\mu)(\gamma+\tau+\mu)(1-\mathcal{R}_v)I.\end{aligned}$$

Then $\dot{\Phi} \leq 0$ when $\mathcal{R}_v \leq 1$ and $\dot{\Phi} = 0$ if and only if $I = 0$ or $\mathcal{R}_v = 1$. For $I = 0$ the first and second equations of (1) show that $M \to M_0, S \to S_0$ and $L, I, R \to 0$ as $t \to \infty$. Hence, Φ is a Lyapunov function on D [8] and so, the largest compact invariant set $\{(M, S, L, I, R) \in D : \dot{\Phi} = 0\}$ is the singleton E_0. Therefore every solution of the model (1), with initial conditions in D approaches E_0 as $t \to \infty$, provided $\mathcal{R}_v \leq 1$ by La Salle's Invariance principle [8].
The above result shows that we can eliminate Hepatitis B from a community if the epidemiological parameter ($\mathcal{R}_v$), can be reduced to a value less than one. ■ □

3.3. **Global stability of EEP.** Here, we prove the global stability of EEP of system (1), assuming that reinfection of recovered individuals is negligible (i.e., $\pi \ll 1$). In such a case, we consider the first four equations of (1) and formulate the following theorem.

Theorem 3.4. *The EEP, E^* of system (1) with $\pi \ll 1$ is globally stable asymptotically in D if $\mathcal{R}_v$ is greater than unity.*

Proof. We define a Lyapunov function $\mathcal{F} : \{(M, S, L, I) : M, S, L, I > 0\} \to \mathbb{R}$ by

$$\begin{aligned}\mathcal{F} = M - M^* - M^* \ln\left(\frac{M}{M^*}\right) + S - S^* - S^* \ln\left(\frac{S}{S^*}\right)\\ + L - L^* - L^* \ln\left(\frac{L}{L^*}\right) + I - I^* - I^* \ln\left(\frac{I}{I^*}\right).\end{aligned}$$

The time derivative of $\mathcal{F}$ computed along the solutions of (1) is then

$$\begin{aligned}\dot{\mathcal{F}} &= \left(1 - \frac{M^*}{M}\right)\dot{M} + \left(1 - \frac{S^*}{S}\right)\dot{S} + \left(1 - \frac{L^*}{L}\right)\dot{L} + \left(1 - \frac{I^*}{I}\right)\dot{I}\\ &= \left(1 - \frac{M^*}{M}\right)[cP - (\phi+\mu)M] + \left(1 - \frac{S^*}{S}\right)[(1-c)P + \phi M - \beta IS - \mu S]\\ &+ \left(1 - \frac{L^*}{L}\right)[\beta IS - (q+k+\mu)L] + \left(1 - \frac{I^*}{I}\right)[kL - (\gamma+\tau+\mu)I].\end{aligned}$$

One can see that, E^* satisfies the following equations.

$$\begin{aligned} &cP = (\phi+\mu)M^*, \;\; (1-c)P = \phi M^* + \beta I^* S^* + \mu S^*, \\ &\beta I^* S^* = (q+k+\mu)L^*, \;\; kL^* = (\gamma+\tau+\mu)I^*. \end{aligned} \tag{12}$$

Using (12), we can write the time derivative of $\mathcal{F}$ as

$$\begin{aligned} \dot{\mathcal{F}} &= \left(1-\frac{M^*}{M}\right)[\phi+\mu-(\phi+\mu)M^*] + \left(1-\frac{S^*}{S}\right)[\phi M^* + \beta I^* S^* + \mu S^* + \phi M - \beta IS - \mu S] \\ &+ \left(1-\frac{L^*}{L}\right)\left(\beta IS - \beta I^* S^* \frac{L}{L^*}\right) + \left(1-\frac{I^*}{I}\right)\left(kL - kL^*\frac{I}{I^*}\right) \\ &= \mu M^*\left(2-\frac{M}{M^*}-\frac{M^*}{M}\right) + \phi M^*\left(1-\frac{MS^*}{M^*S}\right) + \phi M^*\frac{S^*}{S}\left(1-\frac{M^*S}{MS^*}\right) \\ &+ \mu S^*\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right) + \beta IS^*\left(2-\frac{L}{L^*}-\frac{L^*SI}{LS^*I^*}\right) + \beta IS^*\left(2-\frac{S^*I^*}{SI}\right). \end{aligned} \tag{13}$$

Since $S \leq S^*$ and $I \leq I^*$, then (13) becomes

$$\begin{aligned} \dot{\mathcal{F}} &\leq \mu M^*\left(2-\frac{M}{M^*}-\frac{M^*}{M}\right) + \phi M^*\left(2-\frac{MS^*}{M^*S}-\frac{M^*S}{MS^*}\right) \\ &+ \mu S^*\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right) + \beta I^* S^*\left(3-\frac{L}{L^*}-\frac{S^*I^*}{SI}-\frac{L^*SI}{LS^*I^*}\right). \end{aligned}$$

It follows from arithmetic-geometric inequality that

$$\begin{aligned} &\left(2-\frac{M}{M^*}-\frac{M^*}{M}\right) \leq 0, \;\; \left(2-\frac{MS^*}{M^*S}-\frac{M^*S}{MS^*}\right) \leq 0, \\ &\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right) \leq 0, \left(3-\frac{L}{L^*}-\frac{S^*I^*}{SI}-\frac{L^*SI}{LS^*I^*}\right) \leq 0, \end{aligned}$$

so that $\dot{\mathcal{F}} \leq 0$. Hence, by LaSalle's Invariance Principle [8] the endemic equilibrium point E^* is globally asymptotically stable. □

4. Immunization effects

Following [18], we consider the control threshold parameter, $\mathcal{R}_v$ as a function of the fraction of vaccinated new births and the waning rate of the efficacy of vaccine. The vaccine has the effect of reducing the infection rate if the waning rate, ϕ of the efficacy of the vaccine is small. Thus, we assume as in [26] that $\phi = 0$ means the vaccine is completely effective in preventing infection, while $\phi = 1$ means that the vaccine is ineffective. Then, the respective modified vaccination thresholds for such cases are as follows:

$$\mathcal{R}_v(c) = \mathcal{R}_v(c,0) = \frac{\beta k P(1-c)}{\mu(q+k+\mu)(\gamma+\tau+\mu)} \tag{14}$$

and

$$\mathcal{R}_v(c) = \mathcal{R}_v(c,1) = \frac{\beta k P[1+\mu(1-c)]}{\mu(1+\mu)(q+k+\mu)(\gamma+\tau+\mu)}. \tag{15}$$

To compare the impact of vaccination of newborn babies in relation to the waning rate of the efficacy of vaccine, suppose that the HBV invades the population. That is, $\mathcal{R}_0 > 1$ so that E_0 is unstable. For ϕ small enough such an equilibrium point becomes stable again. More precisely, in the vaccination programme, the minimum value for the fraction of newborn babies, c to be vaccinated when the vaccine is completely effective, denoted by c_0 is such that

$$\mathcal{R}_v(c) = \mathcal{R}_v(c,0) = \frac{\beta k P(1-c)}{\mu(q+k+\mu)(\gamma+\tau+\mu)} = 1.$$

Thus

$$c_0 = \frac{1}{\mathcal{R}_0}(\mathcal{R}_0 - 1). \tag{16}$$

Similarly, for an ineffective case, the minimum value for the fraction of newborn babies, c to be vaccinated, denoted by c_1 is such that

$$\mathcal{R}_v(c) = \mathcal{R}_v(c,1) = \frac{\beta k P[1+\mu(1-c)]}{\mu(1+\mu)(q+k+\mu)(\gamma+\tau+\mu)} = 1.$$

This implies that

$$c_1 = \frac{(1+\mu)}{\mu\mathcal{R}_0}(\mathcal{R}_0 - 1) = c_0 + \frac{1}{\mu\mathcal{R}_0}(\mathcal{R}_0 - 1). \tag{17}$$

It follows from (16) and (17), that the minimum value for the fraction of newborn babies need to be vaccinated when the vaccine is completely effective is less than that of ineffective vaccine (i.e., $c_0 < c_1$.)

5. Conclusion

In this note, we review the model of hepatitis B virus proposed by Emereni and Inyama [6] and carry out the rigorous mathematical analysis. We show that model (1) exhibits both a unique non-trivial equilibrium point (E^*) and Disease free equilibrium point (E_0) as presented in [6]. The local and global asymptotic stabilities of these equilibrium points were carried out in relation to the threshold parameter $\mathcal{R}_v$, which determine the disease persistence or otherwise.

This analysis is achieved by linearization theory, Sotomayor theorem [17] and using Lyapunov function in conjunction with LaSalle's Invariance Principle [8]. It is well known that immunization is the most effective strategy for preventing transmission of hepatitis B virus (HBV) infection [3]. It was reported that in high HBV endemic areas, the vaccination strategies in newborns played the most important role in reducing the prevalence of HBV [12]. However, considering the high cost of the HBV vaccine, it is instructive to know the minimum number of newborns required to be immunized especially for developing countries to consider it as a routine component of national immunization programmes. Therefore, we obtain the minimum value of the fraction of newborn babies required to be vaccinated for effective control of the virus. Indeed, the minimum value of such a fraction required to be vaccinated when the vaccine is completely effective (c_0, as presented in (16)) is less than the fraction (c_1, as presented in (17)) required for an imperfect vaccine.

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