Mathematical Model and Analysis of Transmission Dynamics of Hepatitis B Virus

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Abstract

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). In this paper, the transmission dynamics of hepatitis B is formulated with a mathematical model with considerations of different classes of individuals, namely immunized, susceptible, latent, infected, and recovered class. The role of vaccination of new born babies against hepatitis B and the treatment of both latently and actively infected individuals in controlling the spread are factored into the model. The model in this study is based on the standard SEIR model. The disease-free equilibrium state of the model was established and its stability analyzed using the Routh-Hurwitz theorem. The result of the analysis of the stability of the disease-free equilibrium state shows that hepatitis B can totally be eradicated if effort is made to ensure that the sum of the rate of recovery of the latent class, the rate at which latently infected individuals become actively infected and the rate of natural death must have a lower bound.

keywords: Hepatitis B virus (HBV); Disease-free equilibrium; Endemic equilibrium state; Stability analysis

1 Introduction

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). HBV is a DNA virus classified in the virus family of Hepadnaviridae. HBV infection may result in subclinical or asymptomatic infection, acute self-limited hepatitis, or fulminant hepatitis requiring liver transplantation. More than 250 million people are living with hepatitis B virus infection, most of which resulted in more than 800,000 deaths [2]. Hepatitis B (HB) is one of the top infectious diseases known to man, its prevalence is highest in the WHO Western Pacific Region and the WHO African Region.

A vaccine against HB has been available since 1982, nevertheless there is still an increase in the transmission and spread. The HBV can survive outside the body for at least 7 days, during this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. The incubation period of HBV is 75 days on average albeit can vary from 30-180 days. The virus may be detected within 30-60 days after infection and can persist and develop into chronic HB. Majority of the HB carriers do not experience any symptoms during the acute infection phase, however some people have acute illness with symptoms that can last for several day and even weeks. HB progression from latent infection to active disease varies greatly. For instance people with AIDS, or organ transplant are more likely to develop to chronic HB after infection. According to [2] the likelihood that infection becomes chronic can also depend upon the age at which a person becomes infected. Children less than 6 years of age who become infected with the HBV are the most likely to develop to chronic infection.

Mathematical models have been used extensively in researching into not only the dynamical systems in spatial effects [610] but also the epidemiology of HBV disease to improve our understanding of the major contributing factors to the pandemic [3–5]. Anderson and May used a simple mathematical model to illustrate
the effects of carriers on the transmission of HBV. An HBV transmission model was developed to explore the impact of vaccination and other controlling measures for HBV infection. The results shows that booster doses of hepatitis B vaccine are very necessary [6]. In [7], a mathematical model was used to describe the characteristics of HBV disease transmission. The effect of immigrants is analyzed in the model to study the effect of immigrants for the host population.

Motivated by work mentioned above, we use an infectious disease model to understand the role of vaccination and treatment on the transmission dynamics and prevalence of HBV. In this paper, we present the model formulation of the transmission dynamics of HBV, we give the dynamical behaviour of the model including, equilibria and stabilities. This study aims to play a role in the formulation of HB control strategies and establishment of interim goals for intervention programmes

2 Mathematical Model

A variety of mathematical models exist, ranging from stochastic to deterministic (compartmental) model such as: the SIR, SIS, SIRS, SEIS, SEIR, MSIR, MSEIR, and the MSEIRS models (where S=Susceptible class, I=Infective class, M=passively immune infants, E=Exposed class and R=Removed or Recovered class) etc.

The model that is used in this study is deterministic, which takes the form of SEIR where the population is partitioned into components or classes based on the epidemiological state of individuals; and it is assumed that the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic. Therefore, the HP transmission dynamics between the compartments shall be described by a system of differential equation which shall be solved to obtain the disease-free equilibrium state.

3 Basic model assumptions

The model is based on the following assumptions

• That the population is heterogeneous, hence, the individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state.

• That the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic. In other words, that the changes in population of a compartment can be calculated using only history to develop the model.

• That a proportion of the population of newborns is immunized against HB infection through vaccination.

• That the immunity conferred on individuals by vaccination expires after some time at a given rate.

• That the population mixes homogeneously. That is all susceptible individuals are equally likely to be infected by infectious individuals in case of contact.

• That the infection does not confer immunity to the cured and recovered individuals and so they go back to the susceptible class at a given rate

• That people in each compartment have equal natural death rate of $\beta$

• That all newborns are previously uninfected by HBV and therefore join either the immunized compartment or the susceptible compartment depending on whether they are vaccinated or not

• That there are no immigrants and emigrants. The only way of entry into the population is through new-born babies and the only way of exit is through death from natural causes or death from HB-related causes.
3.1 Governing equations

Putting these assumptions together, the model describing HB transmission is formulated as a system of five ordinary differential equations. The dependent variables are $M, S, L, I$ and $R$. At time $t$, $M$ denotes the number of individuals who are immunized against HB through vaccination, $S$ denotes the number of susceptible individuals, $L$ is the number of latently infected/exposed individuals, $I$ represents the number of infectious individuals while $R$ denotes the number of individuals who have been treated and have recovered from the infection. The governing equations read

$$\frac{dM}{dt} = cP - \phi M - \beta M$$  \hspace{1cm} (1)
$$\frac{dS}{dt} = (1 - c)P + \phi M + \pi R - kSI - \beta S$$  \hspace{1cm} (2)
$$\frac{dI}{dt} = kSI - qL - \mu L - \beta L$$  \hspace{1cm} (3)
$$\frac{dI}{dt} = \mu L - \psi I - \eta I - \beta I$$  \hspace{1cm} (4)
$$\frac{dR}{dt} = qL - \psi I - \pi R - \beta R$$  \hspace{1cm} (5)
$$N(t) = M(t) + S(t) + L(t) + I(t) + R(t)$$  \hspace{1cm} (6)

3.2 Model Description

Based on the standard SEIR model, the population is partitioned into 5 compartments or classes namely: Immunized $M(t)$, Susceptible $S(t)$, Latent $L(t)$, Infectious $I(t)$ and Recovered $R(t)$ compartments.

The Immunized component increases due to the coming in of the immunized newborns int the population, where we assumed that a proportion, $cP$, of the incoming individuals are immunized through vaccination. The component reduces due to the expiration of the duration of vaccine efficacy at the rate of $\phi$ and also as a result of natural death at the rate of $\beta$.

The susceptible component of the population grows due to the coming in of new born babies not immunized against HB infection into the population at the rate of $(1-c)P$, the coming in of some recovered individuals due to the fact that the infection does not confer immunity to recovered individuals, at the rate of $\pi$ and as a result of the expiration of the efficacy of the vaccine, at the rate of $\psi$. This component decreases due to the latent infection of individuals at the rate of $k$ and due to death from natural causes at the rate of $\beta$.

The population of the latent component grows as a result of infection of individuals in the susceptible class at the rate of $k$. This class reduces due to the progression of latently infected individuals to active HB infection at the rate of $\mu$, the successful treatment and cure of latent HB patients at the rate of $q$ and as a result of death from natural causes at the rate of $\beta$.

The infectious compartment increases due to the progression of latently infected individuals to active HB infection at the rate of $\mu$. The component reduces as a result of successful cure of infectious HB patients at the rate of $\psi$, death as a result of active HB infection at the rate of $\eta$ and also due to death from natural causes at the rate of $\beta$.

Lastly, the recovered component grows as a result of successful treatment and curer of latent HB patients at the rate of $q$ and that of the infectious HB patient at rate of $\psi$ and decreases due to the fact that recovered individuals are not immunized against the infection and so they return to the susceptible class at the rate of $\pi$ and also as a result of death from natural cause at the rate of $\beta$. 

3
### Table 1: Parameter Description table

| Parameter | Description |
|-----------|-------------|
| $\phi$    | rate of expiration of vaccine efficacy |
| $k$       | rate at which susceptible individuals become latently infected by HB |
| $\mu$     | the rate at which latently infected individuals become actively infected |
| $\psi$    | rate at which actively infected individuals recover from HB infection |
| $\eta$    | HB-induced mortality/death rate |
| $\beta$   | natural mortality/death rate |
| $P$       | population of new births joining the population N |
| $c_\phi$  | the proportion of new births that have been immunized through vaccination |
| $N$       | the total population size |

4 Results and Discussion

4.1 Equilibrium solutions

Let $E(M,S,L,I,R)$ be the equilibrium point of the system described by the equations (1)-(6). At the equilibrium state, we have

$$
\frac{dM}{dt} = \frac{dS}{dt} = \frac{dL}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0.
$$

That is,

1. $cP - \phi M - \beta M = cP - (\phi + \beta)M = 0$ \hspace{5pt} (7)
2. $(1 - c)P + \phi M + \pi R - kSI - \beta S = (1 - c)P + \phi M + \pi R - (kI + \beta)S = 0$ \hspace{5pt} (8)
3. $kSI - qL - \mu L - \beta L = kSI - (q + \mu + \beta)L = 0$ \hspace{5pt} (9)
4. $\mu L - \psi I - \eta I - \beta I = \mu L - (\psi + \eta + \beta)I = 0$ \hspace{5pt} (10)
5. $qL - \psi I - \pi R - \beta R = qL + \psi I - (\pi + \beta)R = 0$ \hspace{5pt} (11)

In order to obtain the disease-free equilibrium state we solve equations (7)-(11) simultaneously. The model can schematically be presented as shown below.

4.2 The Existence of a Trivial Equilibrium State

Let $E_o(M_o, S_o, L_o, I_o, R_o)$ be trivial equilibrium state of the model. There is no trivial equilibrium state for the model since the population cannot be extinct so long as new babies are born into the population. In other words, so long as the recruitment terms $cP$ and $(1 - c)P$ are not zero, the population will never be extinct.

That is, $E_o(M_o, S_o, L_o, I_o, R_o) \neq (0, 0, 0, 0, 0)$

4.3 The Disease-Free Equilibrium State

The disease-free equilibrium state is the state of total eradication of the disease. Let $E^o(M^o, S^o, L^o, I^o, R^o)$ be the disease-free equilibrium state. For disease-free equilibrium state, both the infectious class and the latently infectious class must be zero. That is, for disease-free equilibrium state

$$I^o - L^o = 0 \hspace{5pt} (12)$$

Substituting $I - L = 0$ into equation (7)-(11) and solving simultaneously we have:
From Equation (7)

\[ cP - (\phi + \beta)M = 0 \]

\[ M^o = \frac{cP}{\phi + \beta} \]  \hspace{1cm} (13)

From Equation (8)

\[ (1 - c)P + \frac{\phi cP}{\phi + \beta} + \pi R - \beta S = 0 \]  \hspace{1cm} (14)

From Equation (11)

\[ qL + \psi I - (\pi + \beta)R = 0 \]

\[ \Rightarrow (\pi + \beta)R = 0 \text{(since } L = I = 0) \]

\[ \Rightarrow \text{Either } (\pi + \beta) = 0 \text{ OR } R = 0 \]  \hspace{1cm} (15)

Since \( \pi \) and \( \beta \) are positive constants, \( (\pi + \beta) \neq 0 \)

Therefore, \( R^o = 0 \)

If \( R = 0 \), Equation 14 becomes

\[ (1 - c)P + \frac{\phi cP}{\phi + \beta} - \beta S = 0 \]

\[ \Rightarrow S^o = \frac{(\phi + \beta)(1 - c)P + \phi cP}{\beta(\phi + \beta)} \]

\[ OR \quad S^o = \frac{\phi + \beta - c\beta}{\beta(\phi + \beta)} \]  \hspace{1cm} (17)
Therefore the disease-free equilibrium state of the model is
\[ E^o(M^o, S^o, L^o, I^o, R^o) = \left( \frac{cP}{\phi + \beta}, \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)}, 0, 0, 0 \right) \]

### 4.4 Stability Analysis of the Disease-Free Equilibrium State

To determine the stability or otherwise of the disease-free equilibrium state \( E^o \), we examine the behaviour of the model population near this equilibrium solution. Here we determine the condition(s) that must be met for the disease-free equilibrium state to be stable. In other words, we determine the condition(s) that must be met if the disease is to be totally eradicated from the population.

Recall that the system of equations in this model at equilibrium state is:

\[
\begin{align*}
    cP - (\phi + \beta)M &= 0 \\
    (1 - c)P + \phi M + \pi R - (kI + \beta)S &= 0 \\
    kSI - (q + \mu + \beta)L &= 0 \\
    \mu L - (\psi + \beta + \eta)I &= 0 \\
    qL + \psi I - (\pi + \beta)R &= 0 
\end{align*}
\]

We now linearize the system of equations to get the Jacobian matrix \( J \).

\[
J = \begin{bmatrix}
- (\phi + \beta) & 0 & 0 & 0 & 0 \\
\phi & -(kI^o + \beta) & 0 & -kS^o & \pi \\
0 & kI^o & -(q + \mu + \beta) & kS^o & 0 \\
0 & 0 & \mu & -(\psi + \beta + \eta) & 0 \\
0 & 0 & q & \psi & -(\pi + \beta) \\
\end{bmatrix}
\]

At the disease-free equilibrium, \( E^o(M^o, S^o, L^o, I^o, R^o) \), the Jacobian Matrix becomes

\[
J = \begin{bmatrix}
- (\phi + \beta) & 0 & 0 & 0 & 0 \\
\phi & -\beta & 0 & -k\frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} & \pi \\
0 & kI^o & -(q + \mu + \beta) & k\frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} & 0 \\
0 & 0 & \mu & -(\psi + \beta + \eta) & 0 \\
0 & 0 & q & \psi & (q + \mu + \beta + \lambda) > -(\pi + \beta) \\
\end{bmatrix}
\]

The characteristic equation \(|J_o - I\lambda| = 0\) is obtained from the Jacobian determinant with the Eigen values \( \lambda_i (i = 1, 2, 3, 4, 5) \)

\[
= (\lambda^2 + (\phi + 2\beta)\lambda + (\phi\beta + \beta^2))(-\pi - \beta - \lambda) \begin{bmatrix}
- (q + \mu + \beta) - \lambda & -k\frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} \\
\mu & -(\psi + \beta + \eta) - \lambda \\
\end{bmatrix} = 0
\]
From Equation (21) 

Either

\[(\lambda^2 + (\phi + 2\beta)\lambda + (\phi\beta + \beta^2))(-\pi - \beta - \lambda) = 0 \quad (22)\]

OR

\[
\begin{bmatrix}
-(q + \mu + \beta) - \lambda & -k\frac{\phi + \beta - c\beta}{\beta(\phi + \beta)}
\end{bmatrix}
\begin{bmatrix}
\mu \\
-(\psi + \beta + \eta) - \lambda
\end{bmatrix} = 0 \quad (23)
\]

From Equation (22), we deduce

\[
\lambda_1 = -(\pi + \beta) \quad (24)
\]

\[
\lambda_2 = -\beta \quad (25)
\]

and

\[
\lambda_3 = -(\phi + \beta) \quad (26)
\]

Let

\[
A = \begin{bmatrix}
-(q + \mu + \beta) - \lambda & -k\frac{\phi + \beta - c\beta}{\beta(\phi + \beta)} \\
\mu & -(\psi + \beta + \eta) - \lambda
\end{bmatrix} = 0
\]

For the disease-free equilibrium to be asymptotically stable, \(\text{trace}(A) < 0\) and \(\det A > 0\).

\[
\det A = (q + \mu + \beta + \lambda)(\psi + \beta + \eta + \lambda) - k\frac{\phi + \beta - c\beta}{\beta(\phi + \beta)}
\]

And the trace of \(A\) is:

\[
\text{Trace}(A) = -(q + \mu + \beta + \lambda) - (\psi + \beta + \eta + \lambda)
\]

It is clear that \(\text{trace}(A) < 0\) since all the parameters \(q, t, \beta, \psi, \beta\) and \(\eta\) are positive.

For the determinant of \(A\) to be positive (i.e.\(\neq 0\)), we must have

\[
(q + \mu + \beta + \lambda)(\psi + \beta + \eta) - k\mu\frac{\phi + \beta - c\beta}{\beta(\phi + \beta)} > 0
\]

or

\[
(q + \mu + \beta + \lambda)(\psi + \beta + \eta) > k\mu\frac{\phi + \beta - c\beta}{\beta(\phi + \beta)} \quad (27)
\]

From equation (23)-(25) we see that the first three Eigen values of equation (20) all have negative real parts. We now establish the necessary and sufficient conditions for the remaining two Eigen values of equation (2) to have negative real part. The remaining two Eigen values of equation (20) will have negative real part if and only if \(\det A > 0\). That is, if and only if

\[
(q + \mu + \beta + \lambda)(\psi + \beta + \eta) > k\mu\left(\frac{(\phi + \beta - c\beta)}{\beta(\phi + \beta)}\right)
\]
babies are born. The proportion dynamics of the classes is described using five differential equations.

Presented in this paper is a mathematical model of the role of vaccination and treatment on HB transmission dynamics. The human population under study is partitioned into five classes namely: Immunized, Susceptible, latently infected, Infectious and Recovered classes. It is assumed that the population grows when new babies enter the population, i.e. \( cp + (1-c)P \) cannot be zero and partly because there must always be new born babies entering the population, i.e. new births must have a lower bound. That is, \( (q + \mu + \beta + \lambda) (\psi + \beta + \eta) \) must be less than the total removal rate from both latent and infectious classes given by \((q + \mu + \beta + \lambda) (\psi + \beta + \eta)\).

The Routh-Hurwitz theorem states that the equilibrium state will be asymptotically stable if and only if the product of total contraction and total breakdown of latent class given by \( k\mu \left( \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} \right) \) must be less than the total removal rate from both latent and infectious classes given by \((q + \mu + \beta + \lambda)(\psi + \beta + \eta)\).

Alternatively, the inequality (26) and (27) can also be expressed as

\[
(q + \mu + \beta + \lambda) > k\mu \left( \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)(\psi + \beta + \eta)} \right)
\]

The inequality (28) also gives the necessary and sufficient condition for the stability of the disease-free equilibrium state of the model to be stable. This means that the necessary and sufficient condition for the disease-free equilibrium state of this model to be asymptotically stable is that the product of total contraction and total breakdown of latent class given by \( k\mu \left( \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} \right) \) must be less than the total removal rate from both latent and infectious classes given by \((q + \mu + \beta + \lambda)(\psi + \beta + \eta)\).

The inequality (27) gives the necessary and sufficient condition for the disease-free equilibrium state of this model to be locally asymptotically stable, this is so since the recruitment terms \( cp \) and \( (1-c)P \) cannot be zero and partly because there must always be new born babies entering the population, i.e. \( E_o(M_o, S_o, L_o, I_o, R_o) \) is found to be unstable, this is the state where there is no individual in the population; this is so since the recruitment terms \( cp \) and \( (1-c)P \) cannot be zero and partly because there must always be new born babies entering the population, i.e. \( E_o(M_o, S_o, L_o, I_o, R_o) \neq (0,0,0,0,0) \). The disease-free equilibrium state, \( E^o(M^o, S^o, L^o, I^o, R^o) \), was determined and its stability analysis conducted using the Routh-Hurwitz theorem. The analysis shows that the necessary and sufficient condition for the disease-free equilibrium state to be locally asymptotically stable is that the product of total contraction and total breakdown of the latent class should be less than the total removal rate from both the latent and the infectious classes. That is, \( k\mu \left( \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)} \right) < (q + \mu + \beta + \lambda)(\psi + \beta + \eta) \)

In other words, for the disease-free equilibrium state to be locally asymptotically stable, the sum of recovery rate of the latently infected individuals, the rate at which latently infected become actively infected by the HB disease and natural death rate of individuals in the population must have a lower bound. That is, \( (q + \mu + \beta + \lambda) > k\mu \left( \frac{(\phi + \beta - c\beta)P}{\beta(\phi + \beta)(\psi + \beta + \eta)} \right) \). This establishes the condition under which HB can completely be eradicated in any population.

5 Discussion

Presented in this paper is a mathematical model of the role of vaccination and treatment on HB transmission dynamics. The human population under study is partitioned into five classes namely: Immunized, Susceptible, latently infected, Infectious and Recovered classes. It is assumed that the population grows when new babies are born. The proportion dynamics of the classes is described using five differential equations.
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