Stability Analysis of Mathematical Model of Hepatitis B

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Abstract: In this research study, we developed an MSIR model to understand the effect of combining passive immunisation with treatment of infectious hepatitis B in controlling the spread of hepatitis B. The administration of HBIG vaccines at birth protect children from early infection of hepatitis B but the efficacy of the vaccines expires with time. We established the existence of equilibrium states and analyse the epidemic equilibrium state using Bellman and Cooke’s theorem. We found out that the epidemic equilibrium state is stable when the contact rate is less than 0.8 and becomes unstable at a contact rate 0.8 and above. Hence, effort must be made in bringing down the contact rate and also increasing the duration of efficacy of vaccines used in passive immunisation.

Keywords: Epidemic, equilibrium state, Hepatitis B, immunisation, passive, stability, vaccines

INTRODUCTION

There are five viruses that cause hepatitis, called hepatitis A, B, C, D and E. hepatitis A and E viruses cause infectious hepatitis transmitted by eating food contaminated with faecal material from infected individuals. Viruses B, C and D are called serum hepatitis and are transmitted by contact with blood or body fluids of an infected person. The disease hepatitis B is caused by infection with hepatitis B virus and may lead to unrelieved state. Hepatitis B virus, the most serious type of viral hepatitis (World Health Organization, 2000) can cause acute infection, chronic carrier status and chronic hepatitis. Hepatitis B virus is the only hepatitis virus causing chronic hepatitis that is vaccine preventable.

Hepatitis B virus (HBV) is transmitted through infected blood or body fluids in the same way as human immunodeficiency virus (HIV) although Hepatitis B virus (HBV) is 50-100 times more infectious than human immunodeficiency virus (World Health Organization, 2000). The most common ways of being infected are: from mother-to-baby at birth; child-to-child transmission; through intravenous drug use and through unprotected sexual activity.

Once infected with hepatitis B virus (HBV) there is an incubation period of four to ten weeks; the surface antigen HBsAg then becomes detectable in the blood, with anti-HBe antibodies detectable shortly after (Ganem and Prince, 2004). Another surface antigen, HBeAg, is then released into the blood indicating that the virus is infecting the liver cells and the host is highly infectious. If the infection is going to clear, the levels of antigen HBsAg and HBeAg recede from circulation and the anti-HBs antibodies becomes detected. This is when the patient is classed as immune from further HBV infection. During this period, symptoms of infection may last for several weeks and can include jaundice (yellowing of the skin), fatigue, nausea, vomiting and abdominal pain (World Health Organization, 2000). If the infection does not produce an infective immune response, chronic carrier (CHB) state may develop, where the virus survives and continues to replicate in the body for many years. In this state, the antigen HBsAg remains detectable in the blood for six months after the initial infection (Juszczyk, 2000). The chance of becoming a chronic carrier depends on the age at initial infection: 90% of newborns (up to six months old), 25%-50% of children aged less than 5 years old and 5%-10% of adults who are infected develop CHB (Juszczyk, 2000; World Health Organization, 2000). People with CHB will often have no history of active illness. Patient with CHB may develop cirrhosis (liver scarring) that can lead to liver failure, and they may also develop liver cancer. A small portion (1-6%) of chronic carriers will clear the virus naturally.

THE MATHEMATICAL MODEL

The M-S-I-R model is partitioned into compartments of passively immune infants (M), susceptible individuals (S), infectious individuals (I) and removed individuals (R). The immunised compartment changes due to the coming in of the immunised children into the population where we assumed that a proportion of B of the incoming individuals are immunised against infection. This compartment reduces due to expiration of duration of vaccines efficacy at the rate $\delta$ and also by natural death at the rate $\mu$. 
The susceptible population increases due to the coming of individual from the immunised compartment due to the expiration of duration of vaccines efficacy at the rate $\delta$. The susceptible population also reduces due to natural death at the rate $\mu$ and infection within a contact rate of infection $\beta$.

In the same way the population dynamic of the infectious class grows with the incidence rate of infection $\gamma SI$. This class also reduces by natural death rate $\mu$: and infection within a contact rate of infection $\mu$. Lastly the dynamics of the removed with immunity class increases with successful cure of infectious hepatitis B patients at the rate $\gamma$.

Basic assumptions: The epidemiological features of the hepatitis B virus (HBV) lead to the following assumptions about the transmission of the disease.

- The population has a constant size, $N$ and divided into four and five compartments: MSIR and MSEIR
- The birth and death occur at a constant and equal rate
- The population is mixing in a homogeneous manner i.e. every person has the same chance to becoming in contact with an infected person
- The transmission of the HBV infection occurs at a rate $\beta$.
- Recovery occurs at a rate constant rate $\gamma$.

Keeping in view of these assumptions, our population dynamic, i.e., "passively immune infant- susceptible- infectious- removed" is governed by the following set of differential equations:

\[
\begin{align*}
dM/dT &= B - \delta MS - \mu M \quad (1) \\
dS/dT &= \delta MS - \beta SI - \mu S \quad (2) \\
dl/dT &= \beta SI - \gamma I - \mu I \quad (3) \\
dR/dT &= \gamma I - \mu R \quad (4)
\end{align*}
\]

where, initial population, i.e., $M(0)>0$, $S(0)>0$, $I(0)>0$ and $R(0)>0$ and total population at any instant $t$ is $N(t) = M(t)+S(t)+I(t)+R(t)$.

Now, in the above system (1)-(4), use the following:

\[
\begin{align*}
dM/dt &= dS/dt = dl/dt = dR/dt = 0 \quad \text{and} \\
M(t) &= w, S(t) = x, I(t) = y, R(t) = z
\end{align*}
\]

to get the following re-scaled system:

\[
\begin{align*}
\beta xy - \gamma y - \mu y &= 0 \quad (7) \\
\gamma Y - \mu z &= 0 \quad (8)
\end{align*}
\]

In the next section, we will study the existence of disease free equilibrium state and the epidemic equilibrium state.

Existence of equilibrium states:

Disease free equilibrium state:
The disease free equilibrium state when solved is:

\[
E_1 = (B/\mu, 0, 0, 0) \quad (9)
\]

The epidemic equilibrium state:
The epidemic equilibrium state when solved is:

\[
\begin{align*}
x^*(\gamma + \mu)/\beta \\
w^* &= B\beta/[(\gamma + \beta) + \beta \mu] \\
y^* &= \delta \beta B - \mu(\delta + \gamma + \mu + \beta \mu) \\
z^* &= \gamma \delta \beta B - \mu(\delta + \gamma + \mu + \beta \mu) \gamma
\end{align*}
\]

Hence, the epidemic equilibrium state is:

\[
E^* = (w^*, x^*, y^*, z^*) \quad (14)
\]

DYNAMICAL BEHAVIOUR OF THE SYSTEM

Stability analysis of the epidemic equilibrium state:
We have already established that the system (5)-(8) has disease free equilibrium state, $E_1 = (B/\mu, 0, 0, 0)$ and epidemic equilibrium state $E^* = (w^*, x^*, y^*, z^*)$ in the previous section. Again, the general variational matrix corresponding to the system is given by:

\[
J = \begin{pmatrix}
- (\delta + \mu) & - \delta \beta & 0 & 0 \\
\delta & \delta \beta - \mu & - \beta \gamma & 0 \\
0 & \beta \gamma & \beta \gamma - \mu & 0 \\
0 & 0 & 0 & - \mu
\end{pmatrix}
\]

The characteristic equation is obtained from the Jacobian determinant with the eigen values $\lambda$:

\[
-(\delta + \mu) - \lambda [ (\delta \mu - \beta \gamma + \lambda) (\beta \gamma - \mu) (\mu - \lambda) + \delta \beta \gamma] + \delta \beta \gamma [ (\beta \gamma - \mu) \lambda - \mu] = 0 \quad (16)
\]
Let Eq. (16) take the form:

\[
H(\lambda) = \left[\begin{array}{c}
(\delta v - \beta y - \mu - \lambda) \\
(\delta v - \beta y - \mu - \lambda) \\
(\delta v - \beta y - \mu - \lambda) \\
(\delta v - \beta y - \mu - \lambda)
\end{array}\right]
\]

(17)

Expanding and rearranging in ascending powers of \(\lambda\) we obtained:

\[
H(\lambda) = \lambda^3 + (\delta v + \mu) + \lambda^2 + \lambda + \lambda\]

(18)

We now apply Bellman and Cooke’s theorem to analyze the stability:

Let \(\lambda = iq\)

Substituting Eq. (19) for \(\lambda\) in Eq. (18) we obtained:

\[
H(iq) = \lambda^3 + \lambda^2 + \lambda + \lambda
\]

(20)

Resolving Eq. (20) into real and imaginary parts we obtained:

\[
H(q) = \begin{bmatrix}
\mu(\delta v + \mu) - (\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu)
\end{bmatrix}
\]

(21)

Therefore, \(F(q)\) is

\[
F(q) = 4q^2 - 2q(\delta w - \beta y - \mu) + \mu(\delta w - \beta y - \mu)
\]

(22)

Using Bellman and Cooke’s theorem, we let:

\[
F'(0)G'(0) - F'(0)G(0) > 0
\]

(24)

Now letting \(q = 0\) we obtained:

\[
F(0) = \begin{bmatrix}
\mu(\delta v + \mu) - (\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu)
\end{bmatrix}
\]

(25)

G(0) = 0

(26)

\[
F'(0) = 0
\]

(27)

Substituting Eq. (26) for G(0) and Eq. (27) for \(F'(0)\) in Eq. (24) we obtained:

\[
F(0)G'(0) > 0
\]

(29)

Let \(J = F(0)G'(0)\)

Hence the condition for Eq. (24) to hold is:

\[
J > 0
\]

(30)

Substituting the epidemic state equations in MSIR model into Eq. (25) we obtained:

\[
F(0) = \begin{bmatrix}
\mu(\delta v + \mu) - (\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu) \\
(\delta w - \beta y - \mu)(\delta x + \mu) - \mu(\delta w - \beta y - \mu)(\delta x + \mu)
\end{bmatrix}
\]

(31)

Substituting the epidemic state equations in MSIR model into Eq. (28) we obtained:
Table 1: Stability analysis of the epidemic equilibrium state in msir model using Bellman and Cooke’s theorem

<table>
<thead>
<tr>
<th>B</th>
<th>δ</th>
<th>μ</th>
<th>γ</th>
<th>β</th>
<th>J</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
<td>0.5</td>
<td>0.1</td>
<td>0.0029667</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5</td>
<td>0.2</td>
<td>0.0012419</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.5</td>
<td>0.3</td>
<td>0.0006673</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.4</td>
<td>0.2</td>
<td>0.5</td>
<td>0.4</td>
<td>0.0003796</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.5</td>
<td>0.2</td>
<td>0.5</td>
<td>0.5</td>
<td>0.0002070</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.6</td>
<td>0.2</td>
<td>0.5</td>
<td>0.6</td>
<td>0.0000920</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.7</td>
<td>0.2</td>
<td>0.5</td>
<td>0.7</td>
<td>0.0000099</td>
<td>Stable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.8</td>
<td>0.2</td>
<td>0.5</td>
<td>0.8</td>
<td>-0.0000051</td>
<td>Unstable</td>
</tr>
<tr>
<td>0.2</td>
<td>0.9</td>
<td>0.2</td>
<td>0.5</td>
<td>0.9</td>
<td>-0.0000096</td>
<td>Unstable</td>
</tr>
<tr>
<td>0.2</td>
<td>1.0</td>
<td>0.2</td>
<td>0.5</td>
<td>1.0</td>
<td>-0.0001468</td>
<td>Unstable</td>
</tr>
</tbody>
</table>

Using hypothetical values for the parameters of J we use mathematical software (Maple) to evaluate J and the result is presented in Table 1.

**Theorem 1:** The system (5)-(8) is locally stable around the epidemic equilibrium state $E^*$, when the contact rate is kept below 0.8 and otherwise will make the epidemic equilibrium state unst

\[ G'(0) = \frac{\mu(\gamma + \mu)}{B_0}[\beta(\gamma + \mu + \beta \mu) + \beta \mu] \]

\[ + \mu \delta^2 B\beta + \left(\gamma + \mu\right)(\beta(\gamma + \mu + \beta \mu) + \beta \mu) \]  

(32)

**CONCLUSION**

Government and other immunization partners should strengthen routine HBV immunization programme and effort should be intensified in increasing the duration of efficacy of the vaccines used in passive immunisation programme. Effort should also be intensified towards reducing contact rate to considerable level.

**REFERENCES**


