

Stability Analysis of an Infectious Disease Free Equilibrium of Hepatitis B Model

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Abstract: In this research study, we proposed an (M-S-E-I-R) model to understand the transmission dynamics and control of HBV taking into consideration passive immunisation, treatment of exposed individuals at latent period and infectious Hepatitis B treatment. We established the disease free equilibrium state and epidemic equilibrium state of the model. Stability analysis was carried out on the disease free equilibrium state and it was found that $\lambda_1 = -\mu$, $\lambda_2 = -\mu$, $\lambda_3 = -(\varepsilon+\mu)$, $\lambda_4 = -(\gamma+\mu)$ and $\lambda_5 = \delta B/\mu - \mu$ hence the disease free equilibrium is stable if $\delta B/\mu$ is less than μ (where $\delta B/\mu$ is number of susceptible individuals produced).

Key words: Disease free equilibrium state, epidemic equilibrium state, hepatitis B, infectious diseases, stability analysis

INTRODUCTION

The disease hepatitis B is caused by infection with hepatitis B virus and may lead to unrelieved state. At this time there are at least 350 million persistent carriers of the hepatitis in the world (WHO, 2008). Facts indicate that hepatitis B virus is liable for almost 80 percent of the primary liver cancer, which is one of the most common tumours in man. The most successful way of controlling the infection is vaccination. The availability of vaccine against hepatitis B offers a chance to crack the chain of transmission and prevent keen and continual hepatitis B infections. Hepatitis B virus (HBV) infection is disease of worldwide health. According to the data of world health organization (WHO, 2008) "More than 2,000 million have been infected with HBV at some time in their lives. Of these, about 350, million remain infected chronically and become carrier of the virus. Every year there are over 4 million acute clinical cases of HBV, and about twenty five percent of carriers. Hepatitis B causes about 600,000 people die from chronic active hepatitis, cirrhosis or primary liver cancer annually (WHO, 2008).

The treat of increasing hepatitis B is mainly sexual, household or perinatal exposure to infected person. Avoidance of perinatal HBV transmission is an important step in controlling hepatitis B. Transmission from a HBeAg-positive to her infant may occur in utero, at the time of birth, or after birth. The rate of infection can be as high as 90%. However, neonatal vaccination is highly efficacious (95%). It efficacy indicates that most infections occur at or shortly before birth. On the other hand, caesarean section seems not to be vertically transmitted disease like HIV. The risk of transmission

from mother to infant is related to the HBV replication rate in the mother. There seems to be a direct correction between maternal HBV DNA levels and the likelihood of transmission. In mothers with highly replication HBV, the risk of transmission may be up to 85 to 90%, and it continuously lowers with lower HBV DNA levels Burk *et al.* (1994).

Nigeria is classified among the group of countries highly endemic for hepatitis B virus infection. About 75% of the Nigerian population is reportedly likely to have been exposed to hepatitis B virus at one time or the other in their life Sirisena *et al.* (2002). Co-infection with HBV and HIV is a rapidly growing public health concern. The Sub-Saharan Africa has been most severely affected by the HIV/AIDS pandemic with almost 9% of its adult population leaving with HIV (WHO, 2002, 2003-2007). Mathematical models have played a key role in the formulation of hepatitis B control strategies and the establishment of internal goal for intervention programs. Most of these models are the SEIR class in which the host population is categorized by infection status as susceptible, exposed (infectious but not yet infectious), infectious and recovered. One of the principle attributes of these models is that the force of infection (the rate at which susceptible leave the susceptible class and move into the infected category) is a function of the number of infectious hosts in the population at any time t and is thus, a non linear term. Other transitions such as the recovery of infectious individuals and death are modelled as linear terms with constant coefficients. This study therefore attempts to use mathematical modelling to explain how the spread of hepatitis B can be controlled across Nigeria.

Model description: The M-S-E-I-R model is partitioned into compartments of passively immune infants (M), susceptible individuals (S), exposed individuals in the latent period (E), 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 hepatitis B infection. This compartment reduces due to expiration of duration of vaccine efficacy at the rate δ and also by natural death at the rate μ .

The susceptible population increases due to the coming of individuals from the immunised compartment as a result of the expiration of the duration of vaccines efficacy at the rate δ . The susceptible population also reduces due to natural death rate μ and infection with contact rate of infection β .

The population dynamics of the exposed class at the latent period grows with the incidence rate of βSI . This class reduces by natural death rate μ and occasional break down of the exposed individuals at latent period into infectious hepatitis B at the rate ϵ .

Similarly, the population dynamics of the infectious grows with the occasional breakdown of exposed individuals at the latent period into infectious hepatitis B at the rate ϵ . This class also reduces by natural death rate μ and successful cure of infectious hepatitis B patient at the rate γ and natural death at the rate μ .

Lastly the dynamics of the removed class increases with successful cure of hepatitis B patients at the rate γ and decreases by natural death rate μ . The schematic description of the model is given in Fig. 1.

Model diagram: Keeping in view of these assumptions, our population dynamics i.e., “passively immune infant-susceptible-exposed individuals at latent period-infectious-removed” is governed by the following set of differential equations.

Model equations:

$$\frac{dM}{dT} = B - \delta MS - \mu M \tag{1}$$

$$\frac{dS}{dT} = \delta MS - \beta SI - \mu S \tag{2}$$

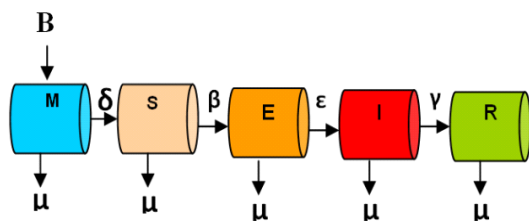


Fig. 1: Schematic representation of the model

$$\frac{dE}{dT} = \beta SI - \epsilon E - \mu E \tag{3}$$

$$\frac{dI}{dT} = \epsilon E - \gamma I - \mu I \tag{4}$$

$$\frac{dR}{dT} = \gamma I - \mu R \tag{5}$$

where, total population at any instant t is $N(t) = M(t) + S(t) + E(t) + I(t) + R(t)$.

Now, in the above system (1) - (5), use the following:

$$\frac{dM}{dt} = \frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0 \text{ and}$$

$$M(t) = v, S(t) = w, E(t) = x, I(t) = y, R(t) = z$$

to get the following re-scaled system:

$$B - \delta vw - \mu v = 0 \tag{6}$$

$$\delta vw - \beta wy - \mu w = 0 \tag{7}$$

$$\beta wy - \epsilon x - \mu x = 0 \tag{8}$$

$$\epsilon x - \gamma y - \mu y = 0 \tag{9}$$

$$\gamma y - \mu z = 0 \tag{10}$$

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

Equilibrium states of the model:

The disease free equilibrium state:

From (7)

$$\delta vw - \beta wy - \mu w = 0$$

$$(\delta v - \beta y - \mu)w = 0$$

$$w = 0 \tag{11}$$

or

$$\delta v - \beta y - \mu = 0 \tag{12}$$

Substituting (11) for w in (8) we obtained:

$$\beta wy - \epsilon x - \mu x = 0$$

$$\beta wy - (\epsilon + \mu)x = 0$$

$$-(\epsilon + \mu)x = 0$$

$$x = 0 \tag{13}$$

Substituting (13) for x in (9) we obtained:

$$\epsilon x - \gamma y - \mu y = 0$$

$$\epsilon x - (\gamma + \mu)y = 0$$

$$\begin{aligned}
 -(\gamma + \mu)y &= 0 \\
 \Rightarrow y &= 0
 \end{aligned}
 \tag{14}$$

Substituting (14) for y in (10) we obtained:

$$\begin{aligned}
 \gamma y - \mu z &= 0 \\
 -\mu z &= 0 \\
 \Rightarrow z &= 0
 \end{aligned}
 \tag{15}$$

Substituting (11) for w in (6) we obtained:

$$\begin{aligned}
 B - \delta v w - \mu v &= 0 \\
 B - \mu v &= 0 \\
 \Rightarrow v &= \frac{B}{\mu}
 \end{aligned}
 \tag{16}$$

Hence the disease free equilibrium state is:

$$E_1 = (B/\mu, 0, 0, 0, 0) \tag{17}$$

The epidemic equilibrium state:

From (9)

$$\begin{aligned}
 \epsilon x - \gamma y - \mu y &= 0 \\
 \epsilon x - (\gamma + \mu)y &= 0 \\
 \epsilon x &= (\gamma + \mu)y \\
 x &= \frac{(\gamma + \mu)y}{\epsilon}
 \end{aligned}
 \tag{18}$$

Substituting (18) for x in (8) we obtained:

$$\begin{aligned}
 \beta w y - (\epsilon + \mu)x &= 0 \\
 \beta w y - \frac{(\epsilon + \mu)(\gamma + \mu)y}{\epsilon} &= 0 \\
 \left[\beta w - \frac{(\epsilon + \mu)(\gamma + \mu)}{\epsilon} \right] &= 0 \\
 y &= 0
 \end{aligned}$$

or

$$\begin{aligned}
 \beta w - \frac{(\epsilon + \mu)(\gamma + \mu)}{\epsilon} &= 0 \\
 \beta w &= \frac{(\epsilon + \mu)(\gamma + \mu)}{\epsilon}
 \end{aligned}$$

$$w^* = \frac{(\epsilon + \mu)(\gamma + \mu)}{\beta \epsilon} \tag{19}$$

Substituting (19) for w in (6) we obtained:

$$\begin{aligned}
 B - \delta v w - \mu v &= 0 \\
 B - (\delta w - \mu)v &= 0 \\
 (\delta w + \mu)v &= B
 \end{aligned}$$

$$v = \frac{B}{(\delta w + \mu)}$$

where,

$$\begin{aligned}
 (\delta w + \mu) &= \frac{\delta[(\epsilon + \mu)(\gamma + \mu)]}{\beta \epsilon} + \mu \\
 (\delta w + \mu) &= \frac{\delta[(\epsilon + \mu)(\gamma + \mu)] + \mu \beta \epsilon}{\beta \epsilon} \\
 \therefore v^* &= -\frac{B \beta \epsilon}{\delta[(\epsilon + \mu)(\gamma + \mu)] + \mu \beta \epsilon}
 \end{aligned}
 \tag{20}$$

From (7)

$$\begin{aligned}
 \delta v w - \beta w y - \mu w &= 0 \\
 \beta w y &= (\delta v w - \mu w) \\
 \beta w v &= (\delta v - \mu)w \\
 \beta y &= (\delta v - \mu)
 \end{aligned}$$

$$y = \frac{(\delta v - \mu)}{\beta} \tag{21}$$

Substituting (20) for v in (21) we obtained:

$$y = \frac{\left[\frac{\delta B \beta \epsilon}{\delta[(\epsilon + \mu)(\gamma + \mu)] + \mu \beta \epsilon} - \mu \right]}{\beta} \tag{22}$$

where,

$$\left[\frac{\delta b \beta \epsilon}{\delta[(\epsilon + \mu)(\gamma + \mu)] + \mu \beta \epsilon} - \mu \right]$$

$$y = \frac{\frac{\delta B \beta \varepsilon \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \mu}{\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon} - \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \mu}{\beta}$$

$$y^* = \frac{\delta B \beta \varepsilon - \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right]}{\left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \beta} \text{ From (22)}$$

Substituting (22) for y in (18) we obtained:

$$x = \frac{(\gamma + \mu)}{\varepsilon} \left[\frac{\delta B \beta \varepsilon - \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \mu}{\beta \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right]} \right]$$

$$x^* = \frac{(\gamma + \mu) \left[\delta B \beta \varepsilon - \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \mu \right]}{\beta \varepsilon \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right]} \text{ (23)}$$

From (10)

$$\begin{aligned} \gamma y - \mu z &= 0 \\ \mu z &= \gamma y \\ \mu &= \frac{\gamma y}{\mu} \end{aligned} \text{ (24)}$$

Substituting (22) for y in (24) we obtained

$$z^* = \frac{\left[\delta B \beta \varepsilon - \left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \mu \right]}{\left[\delta \left[(\varepsilon + \mu)(\gamma + \mu) \right] + \mu \beta \varepsilon \right] \beta \mu} \text{ (25)}$$

Hence the epidemic equilibrium state is given by:

$$E^* = (v^*, w^*, x^*, y^*, z^*)$$

Dynamical behaviour of the system:

Stability analysis of the disease free equilibrium state:

We have already established that the system (6)-(10) has disease free equilibrium state $E_1 = (B/u, 0, 0, 0, 0)$ and epidemic equilibrium state $E^* = (v^*, w^*, x^*, y^*, z^*)$ in the previous section. Again, the general variational matrix corresponding to the system is given by:

$$J = \begin{bmatrix} -(\delta v + \mu) - \lambda & -\delta v & 0 & 0 & 0 \\ \delta v & \delta v - \beta y - \mu - \lambda & 0 & 0 & 0 \\ 0 & \beta y & -(\varepsilon + \mu) - \lambda & \varepsilon & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ -\beta v & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ -(\gamma + \mu) - \lambda & 0 & 0 & 0 & 0 \\ \gamma & -\mu - \lambda & 0 & 0 & 0 \end{bmatrix} \text{ (26)}$$

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

$$-(\delta v + \mu) - \lambda \left[\left(\delta v - \beta y - \mu - \lambda \right) \left(-(\varepsilon + \mu) - \lambda \right) \right] + \left[\left(-(\gamma + \mu) - \lambda \right) \left(-\mu - \lambda \right) \right] + \delta^2 \left[\left(-(\varepsilon + \mu) - \lambda \right) \left(-(\gamma + \mu) - \lambda \right) \left(-\mu - \lambda \right) \right] = 0 \text{ (27)}$$

At the disease free equilibrium state. Substituting (17) into (27) we obtained:

$$\begin{aligned} (-\mu - \lambda) \left(\frac{\delta B}{\mu} - \mu - \lambda \right) \left(-(\varepsilon + \mu) - \lambda \right) &= 0 \\ (-\mu - \lambda) \left(\frac{\delta B}{\mu} - \mu - \lambda \right) \left(-(\varepsilon + \mu) - \lambda \right) &= 0 \\ (-\mu - \lambda)^2 \left(\frac{\delta B}{\mu} - \mu - \lambda \right) \left(-(\varepsilon + \mu) - \lambda \right) &= 0 \\ (-\mu - \lambda) \left(\frac{\delta B}{\mu} - \mu - \lambda \right) &= 0 \\ \lambda_1 &= -\mu \\ \lambda_2 &= -\mu \\ \lambda_3 &= -(\varepsilon + \mu) \\ \lambda_4 &= -(\gamma + \mu) \\ \lambda_5 &= \frac{\delta B}{\mu} - \mu \end{aligned}$$

Note that $\lambda_1, \lambda_2, \lambda_3$ and λ_4 are all negative, the disease free equilibrium will be stable if $\delta B/\mu < \mu$. where, $\delta B/\mu$ is the number of susceptible individuals produced.

Theorem 1: The system (6)-(10) is locally stable around the disease free equilibrium state E_1 , when $\delta B/\mu < \mu$. This implies that the susceptible individuals produce must be less than the natural death rate.

CONCLUSION

It is possible to reduce the risk of perinatal transmission in several ways. The first step is identification of persons at risk. Testing for HBsAg should be performed in all women at the first prenatal visit and repeated later in pregnancy if appropriate. New borns to HBV-positive mothers can be effectively protected by passive immunisation. Hepatitis B immunoglobulin (HBIG) for passive immunisation should be given as early as possible (within 12 h), but can be given up to seven days after birth.

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