Mathematics of Community Public Health Education on Hepatitis B Virus Infection Transmission Control

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Abstract

Chronic Hepatitis B virus remains a significant health problem in sub-Saharan Africa and particularly in Kenya which is classified as high prevalence zone. The prevalence is high in the sub-Saharan Africa and accounts for 80% of the adult patients with hepatitis infection. Morbidity and mortality rates are high due to low disease awareness, absence of treatment protocol and the virulent nature of the disease. A study done in Kisumu County Hospital in Kenya showed that many people are unaware of their infection and infectious state and only come to know of their status at the later stages. A mathematical model based on system of differential equations was therefore developed to study the transmission dynamics of hepatitis B virus infection incorporating public health education. For a disease like hepatitis B virus infection public health education may be fundamental for its control particularly in a situation where effective medicines are already available. The study therefore aimed to evaluate the impact of public health education (PHE) on the spread of hepatitis B virus infection.

1 Introduction

Hepatitis B virus (HBV) is one of the known five hepatitis viruses A, B, C, D and E. Hepatitis B virus (HBV) infection is endemic in the Asia Pacific region and in Africa. Up to 62% of the population in China, up to 98% of the people in sub-Saharan Africa and up to 80% of the populations in some Pacific islands have markers of HBV infection. The infection is spread when body fluid of an infected individual enters the body of a person who is not yet
infected. It can cause both acute and chronic infection. Acute infection may last up to six months with or without symptoms and an infected person is able to pass the virus to others during this time. Chronic hepatitis B infection is developed when someone tests positive for the hepatitis B virus infection after six months of infection. This means that their immune system was not able to clear the hepatitis B virus [12]. 90% of infected newborns and babies will develop chronic infection, up to 50% of infected children between one to five years will develop chronic infection and 5-10% of infected adults will also develop chronic hepatitis B infection[3]. Chronic infection with hepatitis B virus is a common cause of death associated with liver failure, liver cirrhosis and hepatocellular-carcinoma (liver cancer).

It is estimated that one third of the worlds population (approximately 2 billion people) have been infected with hepatitis B at some point of their lives and of these 350-400 million people are chronically infected. Every year about 600,000-1000,000 die from hepatitis B virus infection related disorder [5]. In high endemic regions mother to child transmission accounts for most cases of chronic infections since infection from an infected mother to her infant during delivery is very probable and efficient and is among the most common routes of hepatitis B virus transmission globally.

Many infected individuals show no symptoms (asymptomatic) during the initial infection and in the chronic stage, making them unaware of their infectiousness and of their risk of transmitting the virus to others and of having serious liver disease later in their life. This situation is worsened by the fact that hepatitis B virus infection is highly infectious (50-100 times more) than HIV [5]. Research has shown that 90% of infected adults undergo acute infection with clinical symptoms and subsequently clear the virus. However children who are the majority of infected people have mild or no clinical symptoms immediately after infection and do not clear the virus and hence become chronic carriers. This means many people with HBV chronic infection only begin to seek intervention in the later stages of the infection, the cirrhosis and the hepatocellular carcinoma stages when obvious symptoms develop. This generally means that most of the infected people die due to the complications of hepatitis B virus infection.

2 Study in Kisumu County Hospital

Data collected and analyzed in Kisumu county hospital in Kenya on 257 patient who were diagnosed with hepatocellular carcinoma in 2015 and 2016 showed.
In the two years 100% of those who were diagnosed with liver cancer due to hepatitis B virus infection had not been aware of their hepatitis B infection before they tested Hepatocellular Carcinoma (HCC) positive.

In a control test done on another 257 with symptoms of hepatitis B virus infection the results showed that 179 people were infected with hepatitis B virus, 79 of them were acutely infected and 100 were chronically infected.

Among the infected persons only 7 (2.72%) had done tests earlier and were aware of their hepatitis B positive status while 96.1% had never done test for Hepatitis B virus infection.

This is an indication that many people are infected and spread the disease
without any idea of their infectious status and high rates of transition to cirrhosis and eventually to hepatocellular-carcinoma. Studies have shown that up to 40% of patients with chronic hepatitis B virus infection develop serious complications during their lifetime. Up to 12% of patients with HBV related liver cirrhosis die of liver failure, and up to 10% perish from liver cancer [3, 4].

A different study done in the same county hospital on 180 patients who tested HBV positive gave the following results: 50 people were acutely sick, 40 of them were between 20 years and above, and 10% were 6 years and below. Those who were at liver cirrhosis stage were 70 people in total, 50 of whom were 20 to 50 years old and 20 were those above 50 years old. Those at the liver cancer stage were 60, 40 of them were between 20 and 50 years, and 20 were above 50 years.

The results clearly show that very few children show symptoms of hepatitis B infection during the early stages. Yet most infection occurs in children under six years [cite]. Liver cirrhosis is largely observed in young adults between the age of 20-50 years and a smaller percentage in those above 50 years. This
could be due to the fact that many of those who are infected at birth or in infancy do not exhibit clinical symptoms at the early stage of infection and live with the disease until adulthood when they experience the effects. Similar observations are seen in those who develop hepatocellular carcinoma. Those who progress to liver cancer stage are mostly between the age of 20-50 years. Many of those people who reach cirrhosis stage easily progress to liver cancer stage.

Over the years, it is only been possible to offer patients preventive and supportive care for hepatitis B virus infection. Fortunately, during the last 15 years, effective therapies for chronic infection have emerged. However, despite the existence of a range of interventions such as highly effective infant vaccine to prevent transmission and treat hepatitis B virus infection in early childhood, birth-dose vaccination for prevention of mother-to-child infection, intravenous hepatitis B immunoglobulin and peripartum antiviral therapy for mothers with high viral load, and antiviral treatment for individuals who are already chronically infected, there are still high rates of hepatitis B virus infection and high mortality rates due to its complications.

3 Description and Formulation of the Model

The mathematical model formulated is dynamic and consists of the total human population \( N(t) \) which is sub-divided into classes of susceptible \( S(t) \), acute infected individuals \( I(t) \), chronic infected \( C(t) \), and recovered persons \( R(t) \), hence the total population is given by \( N(t) = S(t) + I(t) + C(t) + R(t) \). Individuals are recruited into susceptible class at the rate of \( \Lambda_H \). Susceptible individuals may acquire hepatitis B virus infection after having sufficient contact with an infected person at the rate of \( \alpha \) where

\[
\alpha = \frac{aI(t) + bdC(t)}{N(t)}
\]

where \( a \) is the rate of effective contact with the acute infected individuals, \( b \) is the rate of effective contact with the chronic infected individuals, \( d \) is the average length of time an individual has stayed with the virus since infection and \( N(t) \) is the total human population. Some of the susceptible individuals may also be vaccinated and join the recovered group at the rate of

\[
q = \frac{(\varphi + \eta)S(t)}{N}
\]

where \( \varphi \) is the efficacy level of public health education, \( \eta \) is the rate of births in hospitals*, \( \mu \) is the natural mortality rate. It is assumed that all those babies
born in the hospital are vaccinated. \( \theta \) is the mortality rate due to disease at acute stage. \( \theta_2 \) is the mortality rate due to disease at chronic stage. Individuals who are in hepatitis B acute status progress to the chronic stage at the rate of \( \beta \) and \( \delta \) is the rate of spontaneous recovery in adults who get infected and are able to fight the virus. \( \gamma \) is the rate at which the chronically ill become better due to treatment, while the acute infected when treated recover at a rate \( \delta \).

4 Determination of the disease-free equilibrium and its stability

The system is investigated for two equilibria states which are the disease-free equilibrium and the endemic equilibrium. At the disease-free equilibrium there is no infection in the population at all, no acute infected person, no chronic carriers, no cirrhosis or cancer cases. Thus the model system has a disease-free equilibrium given by \( D_0 = (S(t), I(t), C(t), R(t)) = (\frac{\Lambda \mu}{\mu}, 0, 0, R(t)) \). The disease-free equilibrium points of a model are steady state solutions in the absence of the disease. The key parameter in epidemic models which identifies important factors in the disease transmission and control is the basic reproduction number, \( R_0[4] \). The reproduction number defined as the number of secondary infection that occurs when an infected individual is introduced in a completely susceptible population during the entire period of his/her infectiousness is one of the important parameters in the analysis of the disease outbreak and it is an important indicator of the level of infectiousness in a population and the effort required to eliminate the infection. If \( R_0 < 1 \) then the outbreak will disappear with time, whereas if \( R_0 > 1 \), then the outbreak will persist at endemic levels. In this case we used the next generation matrix approach to calculate the basic reproduction number.

Since in this study we could not have a perfect situation, the model was formulated based on the following assumptions;

1. The susceptible who are vaccinated join the recovered.
2. Vaccination is also considered as treatment.
3. Those in chronic stage who are treated recover.
4. There is no progression to liver cirrhosis or HCC.
5. All those who are chronically ill and treated recovers.

The compartmental (flow diagram) diagram for the model is given by the figure below.
From the above definition and explanations, the model describing the dynamics of transmission is formulated as

\begin{align*}
S'(t) &= \Lambda_H - qS(t) - \alpha S(t) - \mu S(t) \\
I'(t) &= \alpha S(t) - \beta I(t) - \theta I(t) - \mu I(t) - \delta I(t) \\
C'(t) &= \beta I(t) - \gamma C(t) - \mu C(t) - \theta_2 C(t) \\
R'(t) &= \gamma C(t) + qS(t) - \mu R(t) + (\delta + e)I(t)
\end{align*}

(3)

## 5 Analysis of the model

Based on the fact that (3) monitors living population, all the state variables and parameters are non-negative \( \forall t \geq 0 \) in the feasible region \( \Omega \) where \( S(t), I(t), C(t), R(t) \in \Omega \subset \mathbb{R}^4 \). The solution are bounded in \( \Omega \ \forall \ t \geq 0 \) such that \( N(t) \leq \frac{\Lambda H}{\mu} \) thus the model is epidemiologically well posed in the region \( \Omega \)

### 5.1 Determination of the disease free equilibrium and its stability

In this section we analyzed the model to investigate the stability of its disease free equilibrium. The DFE \((D^0)\) of the model is given by \( D^0 = S(t), I(t), C(t), R(t) = (\frac{\Lambda H}{\mu}, 0, 0, R(t)) \). The DFE points of model are steady states solutions in the absence of the disease. It is the most important equilibrium state for the disease control and its linear stability is governed by the basic reproduction number \( R_0 \). To study the stability of DFE we find the basic reproduction number
$R_0$. It is mathematically defined as the spectral radius of the next generation matrix. It is the number of secondary infection that occurs when an infected individual is introduced into a completely susceptible population [4].

$$FV^{-1}$$

$F$ is Jacobian of $f_i$ where $f_i$ is the rate of appearance of new infection in each compartment and $V$ is the Jacobian of $V_i$ where $V_i$ is the rate of transfer of individual in and out of a compartment by any other means. Hence from the model,

$$F = \begin{pmatrix} \alpha S(t) \\ 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} (\beta + \delta + \theta + \mu)I(t) \\ -\beta I(t) + (\gamma + \theta_2 + \mu)C(t) \end{pmatrix}$$

The matrices $F$ and $V$ from the partial derivatives of $F$ and $V$ with respect to the infected classes computed at DFE are given by:

$$F = \begin{pmatrix} a & bd \\ 0 & 0 \end{pmatrix}$$

and

$$V^{-1} = \begin{pmatrix} \frac{1}{(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)} & 0 \\ \frac{\beta}{(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)} & 1 \end{pmatrix}$$

The eigenvalues of $FV^{-1}$ are $(0, \frac{a}{(\beta + \delta + \theta + \mu)} + \frac{bd\beta}{(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)})$

The basic reproduction number is the spectral radius of the matrix $(FV^{-1})$. That is $\rho(FV^{-1})$ and in this case $R_0$ is

$$R_0 = \frac{a}{(\beta + \delta + \theta + \mu)} + \frac{bd\beta}{(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)}$$

Which is a measure of the severity of an infection.

It’s mathematically stated that the DFE is Locally Asymptotically Stable (LAS) (stability for a small (time) $t$) if $(R_0) < 1$ and unstable if $R_0 > 1$. LAS is stability for a small $t$ which is proved using jacobian matrix of the system (3) at disease free equilibrium $J(D^0)$ by computing the associated trace and determinant and applying the set condition that the trace is negative and determinant is positive for local asymptotic stable.

The jacobian of the full system (3) is

$$J = \begin{pmatrix} -(q + \alpha + \mu) & 0 & 0 & 0 \\ \alpha & -(\beta + \delta + \theta + \mu) & 0 & 0 \\ 0 & \beta & -(\gamma + \theta_2 + \mu) & 0 \\ q & (\epsilon + \delta) & \gamma & -\mu \end{pmatrix}$$
And the jacobian calculated at DFE is given as

$$JD^0 = \begin{pmatrix} -(e + n + \mu) & -a & -bd & 0 \\ 0 & -(a + \beta + \delta + \theta + \mu + e) & -bd & 0 \\ 0 & \beta & -(\gamma + \theta_2 + \mu) & 0 \\ e + n & (e + \delta) & \gamma & -\mu \end{pmatrix}$$

The trace of the matrix at DFE is given by:

$$\text{Tr}(D_0) = -((e + n + \mu) + (a + \beta + \theta + \delta + \mu + e) + (\gamma + \mu + \theta_2)\mu)$$

and the determinant at DFE is given by:

$$\text{Det}(D^0) = \mu(e + n)((\beta + \delta + \theta + \mu) - bd\beta - a(\gamma + \theta_2 + \mu))$$

Substituting $R_0$ it becomes,

$$\mu(e + n)((\beta + \delta + \theta + \mu)(1 - R_0)(\gamma + \theta_2 + \beta))$$

Which is positive whenever $R_0 < 1$. Since the trace is negative and the determinant is positive when $R_0 < 1$ the DFE is therefore locally asymptotically stable.

### 5.2 Global Asymptotic Stability of the DFE

The Global asymptotic stability of the DFE is analyzed based on comparison theorem [11]. The rate of change of the infected can be expressed as;

$$\begin{pmatrix} I'(t) \\ C'(t) \end{pmatrix} = (F - V) \begin{pmatrix} I(t) \\ C(t) \end{pmatrix} - (1 - \frac{S}{N}) \begin{pmatrix} a & bd \\ 0 & 0 \end{pmatrix}$$

Where $F$ and $V$ are as defined earlier in section 0.6.1.

$$F - V = \begin{pmatrix} a - (\beta + \delta + \theta + \mu) & bd \\ \beta & -(\gamma + \theta_2 + \mu) \end{pmatrix}$$

Since $S \leq N \forall t \geq 0$ in $\Omega$, then

$$\begin{pmatrix} I'(t) \\ C'(t) \end{pmatrix} \leq (F - V) \begin{pmatrix} I(t) \\ C(t) \end{pmatrix}$$

From the fact that eigenvalues of matrix $F - V$ all have negative real parts, it follows that the inequality above is stable whenever $R_0 < 1$. Consequently $(I, C) \to (0, 0)$ as $t \to \infty$. Substituting $I = C = 0$ in the system (3) gives $S(t) \to S^0$ as $t \to \infty$, thus $(S(t), I(t), C(t), R(t)) \to (S^0, 0, 0, R)$ as $t \to \infty$ and $D^0$ is GAS if $R_0 < 1$. The results show that with treatment and PHE,
HB infection will be eliminated if $R_0 < 1$. It is established above that DFE is both locally and Globally asymptotically stable whenever $R_0 < 1$ and unstable when $R_0 > 1$. It is noted that with public health education the disease free state can be maintained for a long time without having any infection.

### 5.3 Local stability of endemic equilibrium

A disease is endemic if it is persistent in the population but at controllable levels. The endemic equilibrium point is denoted by $E^*$ where $E^* = (S^*, I^*, C^*, R^*)$. To calculate the EE we set SICR not equal to 0

$$
\Lambda_H - qS(t) - \alpha S(t) - \mu I(t) = 0
$$

$$
\Rightarrow S^* = \frac{\Lambda_H}{(q + \alpha + \mu)}
$$

$$
\alpha I(t) - \beta C(t) - \theta I(t) - \mu I(t) + \delta I(t) = 0
$$

$$
\Rightarrow I^* = \frac{\alpha \Lambda_H}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)}
$$

$$
\beta I(t) - \gamma C(t) - \mu C(t) - \theta_2 C(t) = 0
$$

$$
\Rightarrow C^* = \frac{\beta \alpha \Lambda_H}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)}
$$

$$
\gamma C(t) + qS(t) - \mu R(t) + \delta I(t) = 0
$$

$$
\Rightarrow R^* = \frac{\gamma \beta \alpha \Lambda_H + q(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu) + (e + \delta)(\gamma + \theta_2 + \mu) \alpha \Lambda_H}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)\mu}
$$

Therefore the endemic equilibrium $E^*$ of the model is locally asymptotically stable whenever $R_0 > 1$.

$$
\begin{align*}
\frac{\Lambda_H}{(q + \alpha + \mu)}, & \quad \frac{\alpha \Lambda_H}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)}, & \quad \frac{\beta \alpha \Lambda_H}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)}, \\
\gamma \beta \Lambda_H + q(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu) + (e + \delta)(\gamma + \theta_2 + \mu) \alpha \Lambda_H & \quad \frac{1}{(q + \alpha + \mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)\mu}
\end{align*}
$$

Lemma 0.1 The endemic equilibrium $E^*$ of the model is locally asymptotically stable whenever $R_0 > 1$. 
Proof. The stability of the endemic is investigated by computing the trace and determinant of the jacobian matrix of the system (3), and endemic equation and the jacobian matrix at $E^*$ is given as

$$J = 
\begin{pmatrix}
-q - \alpha - \mu & 0 & 0 & 0 \\
\alpha & -\beta - \delta + \theta + \mu & 0 & 0 \\
0 & \beta & -(\gamma + \theta_2 + \mu) & 0 \\
q & (e + \delta) & \gamma & -\mu
\end{pmatrix}$$

$$J(E^*) = 
\begin{pmatrix}
-(\frac{e+n}{N}r_1 + \frac{ar_2+brdr_3}{N}) + \mu & 0 & 0 & 0 \\
\frac{ar_1+bd}{N} & -(\beta + \delta + \theta + \mu) & 0 & 0 \\
0 & \beta & (\gamma + \theta_2 + \mu) & 0 \\
\frac{(e+n)r_1}{N} & (e + \delta) & \gamma & -\mu
\end{pmatrix}$$

Where; $r_1 = S^* = \frac{\Lambda_H}{(q+\alpha+\mu)}$
$r_2 = I^* = \frac{\alpha \Lambda_H}{(q+\alpha+\mu)(\beta + \delta + \theta + \mu)}$
$r_3 = C^* = \frac{\beta \alpha \Lambda_H}{(q+\alpha+\mu)(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)}$

The trace at EE is given by:
$$\text{Tr}J(E^*) = -(\frac{e+n}{N}r_1 + \frac{ar_2+brdr_3}{N}) + \mu + (\beta + \delta + \theta + \mu) + (\gamma + \theta_2 + \mu) + \mu$$
and the determinant at EE is given by;
$$\text{Det}J(E^*) = \left(\frac{(e+n)r_1}{N} + \frac{ar_2+brdr_3}{N}\right) + \mu(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)$$
Which can be written as
$$\left(\frac{(e+n)r_1}{N} + \frac{ar_2+brdr_3}{N}\right) + \mu(\beta + \delta + \theta + \mu)(\gamma + \theta_2 + \mu)$$
Which remains positive whenever $R_0 > 1$, Therefore EE is locally asymptotically stable.

6 Numerical Simulation

In this section we use numerical simulation in order to give graphical projection of the results of the model (3). Some parameters have been obtained from the literature and some have been assumed or made varying for realistic simulation results. Parameter values are as shown in the table.

The graph below shows the solution of $(S(t), I(t), C(t), R(t))$ individuals against time in days with high success of treatment and PHE, there is low rate of transmission hence $S(t), I(t), C(t)$ decreases over time and $R(t)$ grows exponentially.

Therefore, we conclude that effective treatment of HBV infection incorporating PHE will prevent rapid transmission of the infection.

The results above show that increment of effective treatment and the efficacy level of PHE will result in decrease of HBV infection.

T is treatment
Table 1: Parameter values of the model

<table>
<thead>
<tr>
<th>parameters</th>
<th>symbol</th>
<th>value</th>
<th>source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human recruitment</td>
<td>$\Lambda_H$</td>
<td>$8.748 \times 10^{-3}$ per day</td>
<td>CIA</td>
</tr>
<tr>
<td>Human natural mortality</td>
<td>$\mu$</td>
<td>$2.740 \times 10^{-3}$ per day</td>
<td>CIA</td>
</tr>
<tr>
<td>Mortality rate due to disease</td>
<td>$\theta$</td>
<td>0.004 per year</td>
<td>Estimated</td>
</tr>
<tr>
<td>HB infection rate</td>
<td>$\alpha$</td>
<td>0.00008 per year</td>
<td>Estimated</td>
</tr>
<tr>
<td>Vaccination rate</td>
<td>$q$</td>
<td>0.0000054 per year</td>
<td>Estimated</td>
</tr>
<tr>
<td>Rate of becoming chronic</td>
<td>$\beta$</td>
<td>0.007 per year</td>
<td>Estimated</td>
</tr>
<tr>
<td>Rate of treatment to recovery</td>
<td>$\gamma$</td>
<td>0.25 per year</td>
<td>Estimated</td>
</tr>
<tr>
<td>Rate of spontaneous recovery</td>
<td>$\delta$</td>
<td>0.003</td>
<td>Estimated</td>
</tr>
<tr>
<td>Rate of PHE</td>
<td>$e$</td>
<td>0.05</td>
<td>Estimated</td>
</tr>
<tr>
<td>Modification parameter</td>
<td>$\phi$</td>
<td>$0 &lt; \phi &lt; 1$</td>
<td>Assumed</td>
</tr>
</tbody>
</table>

Figure 6: Numerical simulation

Figure 7: HBV infection, rate of PHE, treatment against time

The results show the infected individuals decreases over a given period of time due the effect of PHE and treatment.

T is treatment
The graph shows that the rate of chronic infection decreases due to effective treatment and PHE.

7 Conclusion

In this study, we developed a mathematical model for hepatitis B infection transmission incorporating treatment and public health education. The results show that DFE of the system is both LAS and GAS. The EE was also found to exhibit LAS. Effective treatment (vaccination and antiviral) are a good control strategy for HB infection, however the study shows that with a combination of effective treatment and PHE the prevalence of HB infection will steadily decline.
8 Recommendation

1. Based on the findings in the research study, we recommend that government should consider training more individuals that will help in PHE of effects, symptoms, causes and danger of HB infection as a control strategy.

2. This study recommends treatment and PHE as a control strategy for HB infection.

References


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