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Modelling the Effects of Public Health Education in the Spread of Hepatitis B Disease

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Abstract

This paper presents a mathematical model that captures some essential dynamics of Hepatitis B transmission to study the impacts of public health educational campaign in preventing the disease. The educational induced reproduction number R_e is compared with the basic reproduction number R_0 to assess the possible benefits to be obtained from this control measure. Numerical results and sensitivity analysis are carried out to support the analytical results and determine the parameters influencing the dynamics of the disease. It is indicated that in the presence of public health education campaign, transmission of infection decreases when people are aware of the disease, implying that the number of acute and chronic infected individuals decrease as well.

Mathematics Subject Classification: 34D20

Keywords: Hepatitis B, public health education, reproduction number

1 Introduction

Hepatitis B is a liver disease that results from infection with Hepatitis B virus (HBV). The disease is usually transmitted when body fluid from a person infected with HBV enters the body of another individual who is not infected. Hepatitis B can be either acute (short term illness) or chronic (a serious disease that can result in long-term health problems and even death). Acute infection

can (though not always) lead to chronic infection (Ciupe *et al.*, 2007). Most people who were infected long ago with HBV are unaware of their chronic infection. They are at high risk of developing severe chronic liver disease and can unknowingly transmit the infection to other people (WHO 2012).

Mathematical models have been used to help understand the transmission dynamics of HBV infections (see Perelson, 2002; Perelson *et al.*, 2005 for reviews). Following these approaches, models were developed to analyze the effects of some interventions against the spread of Hepatitis B infections in the community. For instance, Goldstein *et al.*, (2005) constructed a mathematical model to estimate the impact of vaccination on global Hepatitis B, and the results showed that inclusion of hepatitis B vaccine into infant immunization programme could prevent 80% of HBV related deaths. Also models were developed to analyze the changes in hepatitis B virus levels during drug therapy (e.g. see the following for details, Nowak *et al.*, 1996; Tsiang *et al.*, 1999; Lau *et al.*, 2000; Shoujun *et al.*, 2000; Lewin *et al.*, 2001; Colombatto *et al.*, 2006; O'leary *et al.*, 2010; Momoh *et al.*, 2012).

Hepatitis B disease impose a heavy burden on the health care system because of the costs of treatment of liver failure and chronic liver disease. In many countries, Hepatitis B is the leading cause of liver transplants. Such end-stage treatments are expensive, easily reaching up to hundreds of thousands of dollars per person. People who are chronically infected can spread hepatitis B Virus to others, even if they do not look or feel sick (Sleisenger *et al.*, 2006). Public Health education campaign may help to improve the health and well being of people in local communities and around the globe. Public health professionals may help to prevent health problem before they occur by implementing educational programmes, developing policies, administering services, regulating health systems and conducting researches. These non-pharmaceutical interventions such as the use of public health education campaigns are vital by creating awareness to people about the disease. In this paper a mathematical model is formulated to study the role of public health education in curtailing the spread of hepatitis B disease. It is anticipated that public health education programme can have major effect in reducing the transmission dynamics of the disease in a homogeneous population.

2 Model Formulation

An HBV model classifies the human population at time t, denoted by $N(t)$ into the following mutually exclusive sub-populations: susceptible individuals ($S_i(t)$), acute infected individuals ($A_i(t)$) and chronic infected individuals ($C_i(t)$), where $i = (u, e)$ with $i = u$ denoting uneducated individuals and $i = e$ denoting educated individuals. Here, uneducated means individuals who do not receive proper public health education or counselling against risky prac-

tices that may result into HBV transmission. It is assumed that susceptible individuals are recruited into the population at a constant rate Λ. A proportion p of these newly recruited individuals is assumed to be educated about the disease (categorized in the S_e class) and the complementary proportion $(1-p)$ are uneducated and are categorized in S_u class. Uneducated susceptible individuals get educated about the disease at a constant rate α_1 due to public health education against HBV.

Educated susceptible individuals (S_e) and uneducated susceptible individuals (S_u) acquire HBV infection following effective contact with infectious individuals at rates λ_e and λ_u respectively. We also assume that educated infected individuals (in acute class or chronic class) modify their behaviour positively, thereby reducing their risk of HBV transmission by a factor ϵ, with $0 < \epsilon < 1$. In other words, it is assumed that HBV infected individuals who receive public health education transmit the disease at a lower rate in comparison to uneducated HBV infected individuals. It is assumed that the efficacy of public health education in preventing new infection among educated susceptible individuals is φ, where $\varphi \in [0, 1]$. Thus, educated susceptible individuals acquire infection at a reduced rate $(1-\varphi)[\lambda_u + (1-\epsilon)\lambda_e]$, and uneducated susceptible individuals acquire infection at the rate $\lambda_u + (1-\epsilon)\lambda_e$. Uneducated individuals who are at acute stage progress to chronic at a rate γ_u, while educated acute infected individuals progress to chronic at reduced rate γ_e, so $\gamma_e < \gamma_u$. That is, acute infected individuals who receive public health education programme progress to chronic at a slower rate than those who do not.

Uneducated infected acute individuals are educated at a rate α_2 and move to the corresponding educated acute class. Individuals in all classes suffer natural death at a rate μ. Additionally, individuals with chronic HBV die at a rate σ_u (for the uneducated class) or σ_e (for the educated class) such that $\sigma_e < \sigma_u$. Thus, it is assumed that chronic HBV patients who receive public health education die due to disease at a slower rate than chronic HBV patients who do not. Uneducated HBV individuals in chronic class (C_u) are educated at a rate α_3 and move to the corresponding educated HBV chronic class (C_e). A schematic diagram of the model is shown in Figure 1.

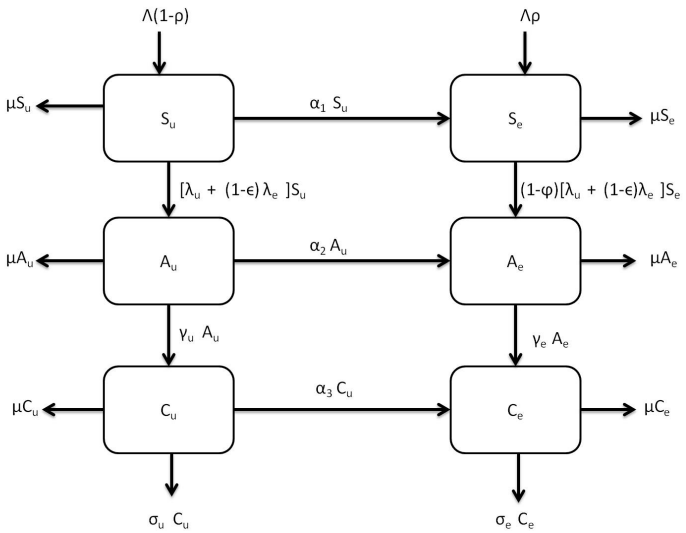


Figure 1: Compartmental HBV model with public health education

2.1 HBV Model

Putting the formulations and assumptions together gives the following system of nonlinear differential equations:

$$\begin{aligned}
\frac{dS_u}{dt} &= \Lambda(1-\rho) - \mu S_u - \alpha_1 S_u - [\lambda_u + (1-\epsilon)\lambda_e]S_u, \\
\frac{dS_e}{dt} &= \Lambda\rho + \alpha_1 S_u - \mu S_e - (1-\varphi)[\lambda_u + (1-\epsilon)\lambda_e]S_e, \\
\frac{dA_u}{dt} &= [\lambda_u + (1-\epsilon)\lambda_e]S_u - (\mu + \alpha_2 + \gamma_u)A_u, \\
\frac{dA_e}{dt} &= (1-\varphi)[\lambda_u + (1-\epsilon)\lambda_e]S_e + \alpha_2 A_u - (\mu + \gamma_e)A_e, \\
\frac{dC_u}{dt} &= \gamma_u A_u - (\mu + \alpha_3 + \sigma_u)C_u, \\
\frac{dC_e}{dt} &= \gamma_e A_e + \alpha_3 C_u - (\mu + \sigma_e)C_e,
\end{aligned} \tag{2.1}$$

where $\lambda_u = \frac{\beta(A_u + \delta_u C_u)}{N}$ and $\lambda_e = \frac{\beta(A_e + \delta_e C_e)}{N}$ are forces of infection from uneducated and educated infected idividuals respectively. The parameter β,represents the effective contact rate that may result in the transmission of HBV infection, while the parameters $\delta_u > \delta_e > 1$ account for the relative infectiousness of uneducated and educated infections individuals respectively. The initial conditions for the model system (1.1) are $S_u(0) > 0, S_e(0) > 0, A_u(0) \geq 0, A_e(0) \geq 0$, $C_u(0) \geq 0, C_e(0) \geq 0$.

2.2 Existence of Solutions

The model system (2.1) describes the dynamics of human population in the presence of HBV infection. All the model variables are non-negative. Hence,

model (2.1) is biologically and mathematically well posed in the closed set

$$\Phi = \left\{ (S_u, S_e, A_u, A_e, C_u, C_e) \in \mathbb{R}^6_+ : N \leq \frac{\Lambda}{\mu} \right\}, \tag{2.2}$$

which is a positively invariant and attracting in the domain of Φ.

3 Analysis of the HBV Sub-models

3.1 The Basic HBV Model

This is obtained when $\rho = \alpha_1 = \alpha_2 = \alpha_3 = \gamma_e = \sigma_e = \epsilon = \varphi = 0$. Thus, model (2.1) reduces to

$$\begin{array}{l} \frac{dS}{dt} = \Lambda - (\lambda + \mu)S, \\ \frac{dA}{dt} = \lambda S - (\gamma + \mu)A, \\ \frac{dC}{dt} = \gamma A - (\sigma + \mu)C, \end{array} \tag{3.1}$$

where the force of infection $\lambda = \frac{\beta(A+\delta C)}{N}$ and $N(t) = S(t) + A(t) + C(t)$. The set
$\Phi = \left\{ (S(t), A(t), C(t)) \in \mathbb{R}^3_+ : N(t) \leq \frac{\Lambda}{\mu} \right\}$ attracts all solutions in $\mathbb{R}^3_+$.

3.1.1 Disease-Free Equilibrium and Stability

The disease free equilibrium (DFE) is the most important equilibrium state for disease control, and its linear stability is governed by the basic reproduction number R_0 (see e.g Hethcote 2000; Diekmann *et al.*, 1990; Castillo-Chavez *et al.*, 2002), mathematically defined as the spectral radius of the next generation matrix. It is a unitless threshold quantity for the disease control which defines the number of secondary infections produced by a single infected individual in a completely susceptible population. The disease-free equilibrium (DFE) of the HBV basic model (3.1) is given by

$$E_0 = (S^*, 0, 0) \;=\; \left(\frac{\Lambda}{\mu}, 0, 0 \right).$$

Applying the notations as in Van den Driessche and Watmough (2002) for the model system (2.1), the matrices F and V for the new infection terms and the remaining transfer terms are respectively given by

$$F \;=\; \begin{bmatrix} \frac{\beta\mu(1-\rho)}{A_1} & (1-\epsilon)\frac{\beta\mu(1-\rho)}{A_1} & \frac{\beta\delta_u\mu(1-\rho)}{A_1} & (1-\epsilon)\frac{\beta\delta_e\mu(1-\rho)}{A_1} \\ (1-\varphi)\frac{\beta A_6}{A_1} & A_7\frac{\beta A_6}{A_1} & (1-\varphi)\frac{\beta\delta_u A_6}{A_1} & A_7\frac{\beta\delta_e A_6}{A_1} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \tag{3.2}$$

and

$$V = \begin{bmatrix} A_2 & 0 & 0 & 0 \\ -\alpha_2 & A_5 & 0 & 0 \\ -\gamma_u & 0 & A_3 & 0 \\ 0 & -\gamma_e & -\alpha_3 & A_4 \end{bmatrix}, \tag{3.3}$$

where $A_1 = \mu + \alpha_1$, $A_2 = \mu + \alpha_2 + \gamma_u$, $A_3 = \mu + \alpha_3 + \sigma_u$, $A_4 = \mu + \sigma_e$, $A_5 = \mu + \gamma_e$, $A_6 = \mu\rho + \alpha_1$, $A_7 = (1 - \varphi)(1 - \epsilon)$.

The basic reproduction number for the basic HBV model denoted by R_0 is

$$R_0 = \rho(FV^{-1}) = \frac{\beta[(\sigma_u + \mu) + \delta_u\gamma]}{(\gamma + \mu)(\sigma_u + \mu)}. \tag{3.4}$$

Thus, using Theorem 2 of Van de Driessche and Watmough (2002) the following result was established.

Theorem 3.1 *The DFE of the model system (3.1) is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

The basic reproduction number measures the average number of new infections generated by a single infected individual in a completely susceptible population. Lemma 3.1 implies that HB disease can be eliminated from the community (when $R_0 < 1$) if the initial sizes of the sub-populations of the model are in the basin of attraction of the disease-free equilibrium.

3.2 HBV Model with Public Health Education

Individuals at risk are sensitized through intensive public health education to participate fully in the following activities: Avoiding unsafe sexual intercourse, unsafe blood transfusion, use of contaminated injection during medical procedures, and sharing of needles and syringes among injecting drug users. Educators may use appropriate local media such as radio, television or newspapers in disseminating health education messages to the general public. The model system (2.1) incorporates public educations campaigns and the analysis is done in the positively invariant region Φ.

3.2.1 Disease-Free Equilibrium and Local Stability

The disease-free equilibrium of the model (2.1) is given by

$$E_0^* = (S_u^{**}, S_e^{**}, A_u^{**}, A_e^{**}, C_u^{**}, C_e^{**}) = \left\{ \frac{\Lambda(1-\rho)}{\mu + \alpha_1}, \ \frac{\Lambda(\mu\rho + \alpha_1)}{\mu(\mu + \alpha_1)}, 0, 0, 0, 0 \right\}. \tag{3.5}$$

For the model system (2.1), the next generation matrix calculation (Van den Driessche and Watmough, 2002) shows that the education-induced reproduction number R_e is

$$R_e = \frac{\beta(G_1+G_2+G_3)}{(\mu+\alpha_1)K_2K_3K_4K_5} = \frac{(\gamma+\mu)(\sigma_u+\mu)R_0}{\sigma_u+\mu+\delta_u\gamma}\left\{\frac{(G_1+G_2+G_3)}{(\mu+\alpha_1)K_2K_3K_4K_5}\right\}, \tag{3.6}$$

where $K_2 = \mu+\alpha_2+\gamma_u$, $K_3 = \mu+\alpha_3+\sigma_u$, $K_4 = \mu+\sigma_e$, $K_5 = \mu+\gamma_e$, $G_1 = \mu K_4K_5(1-\rho)[K_3+\delta_u\gamma_u]$, $G_2 = \mu(1-\epsilon)(1-\rho)[\alpha_2K_3K_4+\delta_e(\alpha_3\gamma_uK_5+\alpha_2\gamma_eK_3)]$, $G_3 = K_2K_3(\mu\rho+\alpha_1)(1-\epsilon)(1-\varphi)[K_4+\delta_e\gamma_e]$, and R_0 is as in Equation (3.4). From Theorem 2 in Van den Driessche and Watmough (2002), we have the following result.

Theorem 3.2 *The DFE of the model system (3.1) is locally asymptotically stable if $R_e < 1$ and unstable if $R_e > 1$.*

Biologically speaking, Lemma (3.2) implies that hepatitis B may be prevented from the community with education as a control strategy (when $R_e < 1$) if the initial sizes of the sub-populations of the model are in the region of of attraction of the disease-free equilibrium.

3.2.2 Global Stability of Disease-Free Equilibrium

We have the following result on the global stability of the disease-free equilibrium

Theorem 3.3 *If $R_e < 1$,the disease free equilibrium point is globally asymptotically stable and unstable if $R_e > 1$.*

Proof
By the comparison theorem, the rate of change of the variables representing the infected components of model system (2.1) can be re-written as,

$$\begin{bmatrix} A_u' \\ A_e' \\ C_u' \\ C_e' \end{bmatrix} = (F-V)\begin{bmatrix} A_u \\ A_e \\ C_u \\ C_e \end{bmatrix} - \begin{bmatrix} (\lambda_u+(1-\epsilon)\lambda_e)S_u \\ (1-\varphi)(\lambda_u+(1-\epsilon)\lambda_e)S_e \\ 0 \\ 0 \end{bmatrix}, \tag{3.7}$$

where the matrices F and V in are defined as

$$F = \begin{bmatrix} \frac{\beta\mu(1-\rho)}{A_1} & (1-\epsilon)\frac{\beta\mu(1-\rho)}{A_1} & \frac{\beta\delta_u\mu(1-\rho)}{A_1} & (1-\epsilon)\frac{\beta\delta_e\mu(1-\rho)}{A_1} \\ (1-\varphi)\frac{\beta A_6}{A_1} & A_7\frac{\beta A_6}{A_1} & (1-\varphi)\frac{\beta\delta_u A_6}{A_1} & A_7\frac{\beta\delta_e A_6}{A_1} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and

$$V = \begin{bmatrix} \mu+\alpha_2+\gamma_u & 0 & 0 & 0 \\ -\alpha_2 & \mu+\gamma_e & 0 & 0 \\ -\gamma_u & 0 & \mu+\alpha_3+\sigma_u & 0 \\ 0 & -\gamma_e & -\alpha_3 & \mu+\sigma_e \end{bmatrix}.$$

Hence, we have

$$\begin{bmatrix} A_u^{'} \\ A_e^{'} \\ C_u^{'} \\ C_e^{'} \end{bmatrix} \leq (F-V) \begin{bmatrix} A_u \\ A_e \\ C_u \\ C_e \end{bmatrix}. \tag{3.8}$$

Furthermore, having all the eigenvalues of the matrix $F-V$ with negative real parts, the result is that the inequality (4.30) is stable for $R_e < 1$. Also it follows that $(A_u^{**}, A_e^{**}, C_u^{**}, C_e^{**}) \to (0,0,0,0)$ as $t \to \infty$. By comparison theorem it follows that $(A_u^{**}, A_e^{**}, C_u^{**}, C_e^{**}) \to (0,0,0,0)$ as $t \to \infty$. The first, second, third, fourth,fifth, and the sixth equations of the system (4.1), gives $S_u = \frac{\Lambda(1-\rho)}{(\mu+\alpha_1)}$ and $S_e = \frac{\Lambda(\mu\rho+\alpha_1)}{\mu(\mu+\alpha_1)}$ whenever$A_u^{**} = A_e^{**} = C_u^{**} = C_e^{**} = 0$. Thus $(A_u^{**}, A_e^{**}, C_u^{**}, C_e^{**}) \to E_0^*$ as $t \to \infty$ for $R_e < 1$.Hence, the disease free equilibrium point E_0^* is globally asymptotically stable.

3.2.3 Effect of Public Health Education Campaigns

The reproduction number is a measure of the ability of the disease to invade a population under conditions that facilitate maximal growth. Reconsidering the education -induced reproduction number as

$$R_e = R_0 M_1,$$

where

$$M_1 = \frac{(\gamma+\mu)(\sigma_u+\mu)}{\sigma_u+\mu+\delta_u\gamma}\left\{\frac{(G_1+G_2+G_3)}{(\mu+\alpha_1)K_2K_3K_4K_5}\right\},$$

and using the model parameters values given in Table 2, it can be shown that $M_1 < 1$ for some suitably chosen parameter values, implying that $R_e < R_0$. Thus M_1 is the factor by which public health education campaigns reduce the number of secondary infections in a community.

4 Numerical Simulations

Numerical simulations of model system (2.1) were carried out using a set of parameter values given in Table 2. Matlab ODE solvers was used in the numerical simulations.

Table 1: The sensitivity indices of the effective reproduction number R_e

Parameter	Sensitivity Index
ϵ	-44.30896917
φ	-1.332791662
β	0.999996052
δ_e	0.495365233
μ	-0.316468869
σ_e	-0.304840459
γ_e	-0.1915729
ρ	-0.14638067
α_1	-0.09383355
δ_u	0.076928224
σ_u	-0.041390951
α_3	-0.033775909
α_2	-0.012120357
γ_u	-0.00594130049

4.1 Sensitivity analysis

Sensitivity analysis is used to determine the relative importance of model parameters to HBV transmission and its prevalence. The analysis is performed by computing the sensitivity indices of the effective reproduction number R_e. According to Chitnis *et al.*, (2008), sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values. Sensitivity analysis determines parameters which have high impact on the education induced (effective) reproduction number R_e, and can be used to measure the relative change in the R_e to the relative change in the parameter. Using a set of reasonable parameter values given in Table 2, sensitivity indices were calculated. The negative sign of the sensitivity indices means that the increase in the corresponding parameter value leads to a decrease of the effective reproduction number R_e. The sensitivity indices are shown in Table 1.

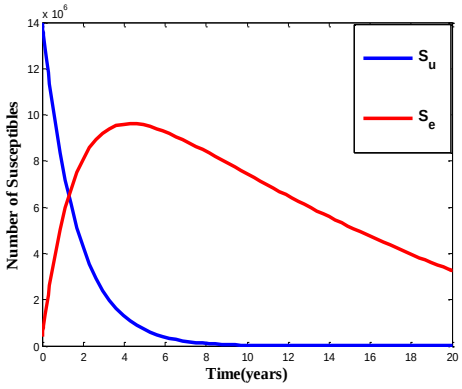
4.1.1 Impacts of Public Health Education Campaign

Numerical simulations of the HBV model system (2.1) showing the time series plots of uneducated and educated susceptible individuals (Fig. 2(a)), uneducated and educated acute infected individuals (Fig. 2(b)) and uneducated and educated chronic infected individuals (Fig. 2(c)). Numerical results in Figure 2(a), (b) and (c) illustrate that an increase in public health education campaign on HBV will generally result in an increase in the number of educated susceptible individuals, educated acute infected individuals and educated chronic infected individuals. The figure shows that significant changes are observed in the initial stages of the epidemic with more changes being observed

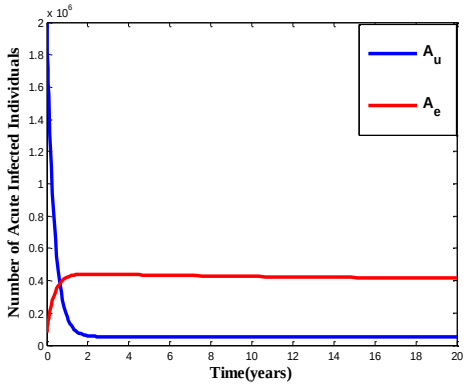
Table 2: Parameter Values and their interpretations

Parameter Description	Symbol	Value	Source
Recruitment rate	Λ	70	Gumel.,(2003)
Reduction factor to infection	ϵ	0.98	Momoh *et al.*,(2012)
Efficacy of education	φ	0.6	Estimate
Effective contact rate	β	0.5	Estimate
The modification parameter	δ_u, δ_e	$1.5, 1.3$	Estimate
HBV related death rate	σ_e	0.04	Estimate
Progression rate from A_e to C_e	γ_e	0.05	Estimate
Natural mortality rate	μ	0.02	Ciupe *et al.*,(2007)
HBV related death rate	σ_u	0.47	Nowak and May.,(2000)
Progression rate from A_u to C_u	γ_u	2.7	Estimate
Rate of becoming educated from S_u to S_e	α_1	0.5	Estimate
Rate of becoming educated from A_u to A_e	α_2	0.51	Estimate
Rate of becoming educated from C_u to C_e	α_3	0.5	Estimate
Fraction of educated newly recruited individuals	ρ	0.6	Estimate

in educated susceptible individuals and educated chronic infected individuals.



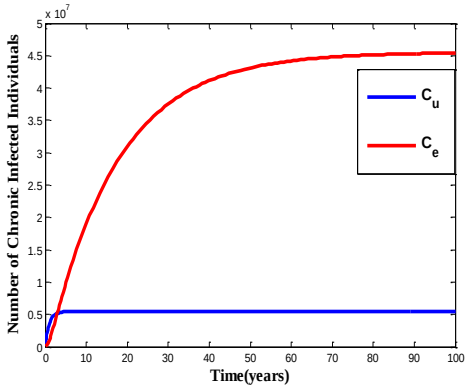
(a)



(b)

4.1.2 Effects of varying some parameters

In Figure 3, the effects of varying φ and α_1 on R_e is illustrated using parameter values in Table 2. The illustration in Figure 3, shows that the increased efficacy of education campaign α_1, against HBV results in an increase of R_e and so in an increase of α_1. Thus, an increase of the education efficacy increases the



(c)

Figure 2: Simulation results showing the changes in the six state variables of the HBV model with public health education programme in pairs such as (a) Uneducated and educated susceptible individuals, (b) Uneducated and educated HBV acute infected individuals and (c) Uneducated and educated chronic infected individuals of the model system (2.1) where $R_0 = 1.70318$ and $R_e = 0.126645$.

number of secondary infections and so the influx of individuals in HBV infected communities.

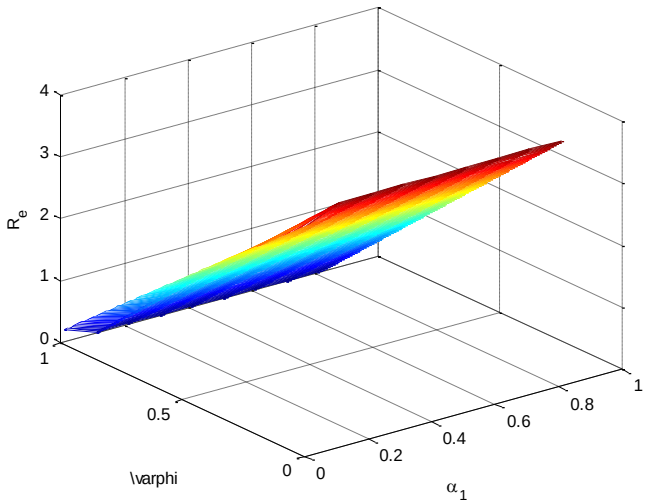


Figure 3: Plot showing the effect of varying φ and α_1 on the reproduction number R_e using parameter values from Table 2

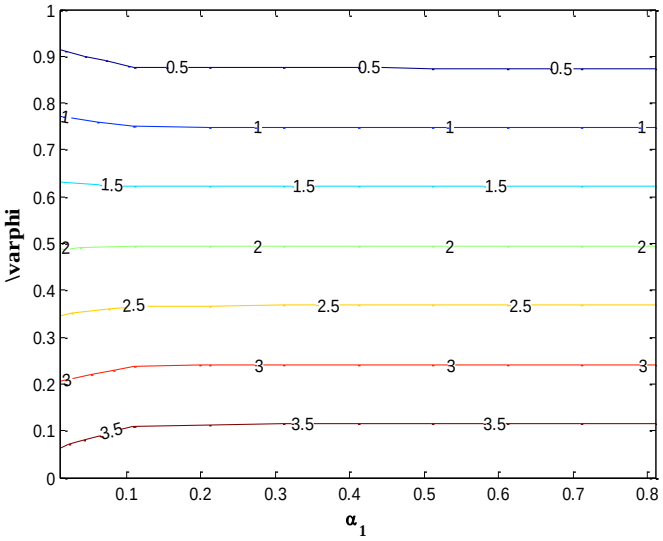


Figure 4: Contour plots of R_e as a function of φ and α_1

Figure 4, shows that the increase of φ which is the efficacy of education programme in reducing more infectious, results in a decrease in the effective reproduction number,R_e regardless of whatever the value of α_1 which is the rate of becoming educated. It implies that good campaigns and enough education has positive impact on the reduction of HBV transmission.

5 Conclusion

A mathematical model for HBV incorporating public health education classes in a community is presented as a system of differential equations. The existence of solutions has been discussed and that the domain of the system is epidemiologically and mathematically well posed. It was shown that the model system has a disease free equilibrium which is locally and globally asymptotically stable. Numerical results suggest that an increase in the rate of providing health education against HBV disease may generally result in the increase of the number educated susceptible individuals. Based on the results of the study, we conclude that the most effective way to reduce the transmission of HBV epidemic infection is to educate people to go for checkup and become aware of their HBV status. Furthermore people should be educated to be aware of the consequences of practicing unsafe sex and other preventive measures against the infection. Policy makers should strive to sensitize the general public to voluntarily go for screening. Finally, because of the complication of HBV disease in terms of different transmission level and different immunological status prevalent in different location, some guidelines should be developed to give

researchers and health professionals a more accurate foundation on developing the appropriate vaccines.

The model developed in this paper is not fully realistic, but it is believed that it can capture some relevant properties also valid in more complex HBV infection models. For example, to make the model more realistic, the community can be considered to consist of individuals of different types, assuming that HBV transmission depends on the type of individuals. For instance, it would be interesting to investigate the effect of public health education campaign in the community made up of different infectivity and susceptibility to hepatitis B disease.

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