



A Graph-Theoretic Method on HBY Epidemic Model

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Abstract

In this paper, we present an epidemic model with non-monotonic incidence function. This epidemic model is investigated for different classes of infectious diseases. Mathematical analyses are carried out to determine the positivity of solution and the Graph-Theoretic method is used in calculating the Basic reproduction number. In addition, we obtained the numerical simulation to verify the model predictions. The results suggested that the model is approaching equilibrium with increase immunization program.

Keywords: Hepatitis B, Endemic, Equilibrium, Pathogens.

Introduction

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV), Edmund *et. al.* (1993). It is a major global health problem and the most serious type of viral hepatitis. Originally known as “serum hepatitis”, the disease has caused epidemics in parts of Asia and Africa, and it is endemic in China, Williams (2006). About a third of the world population has been infected at one point in their lives, including 350 million who are chronic carriers which causes 620,000 deaths worldwide each year, World Health Organization Report (2004). If the body is able to fight off the hepatitis B infection, any symptoms should go away over a period of weeks to months, this is termed acute hepatitis B. some individual's bodies are not able to completely get rid of the hepatitis B infection. This is called chronic hepatitis B. In many developed countries (e.g. those in Western Europe and North America), patterns of transmission are different from those in developing countries. The majority of infections in developed countries are transmitted during young adulthood by sexual activity, tattoo or acupuncture with unclean needles and instruments, and injecting drug use, Gane (2005). Hepatitis B is a major infectious occupational hazard of health workers, Barker *et. al.* (1996). The hepatitis B virus is not spread by contaminated food or water, and cannot be spread casually in the workplace, McManhon *et. al.* (1985).

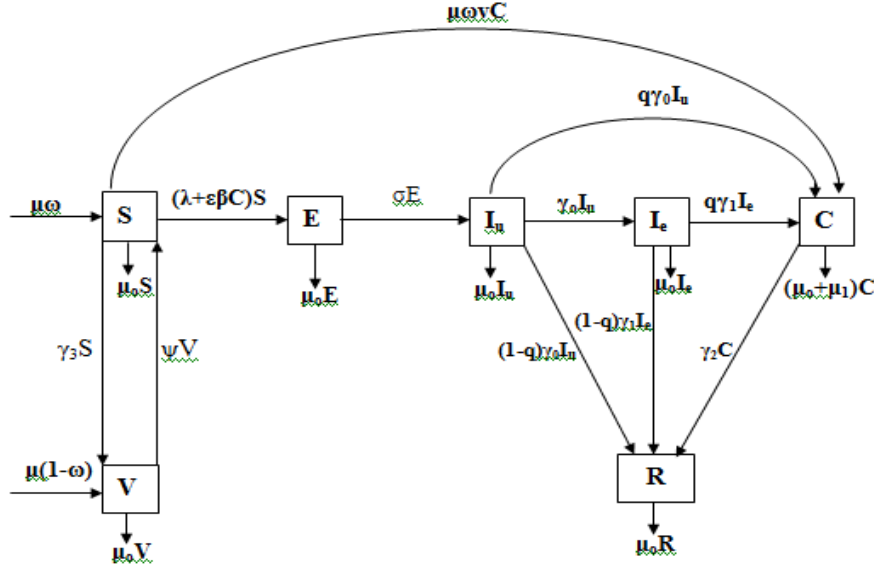


Figure 1: Schematic representation of interactions of HBV transmission

Mathematical Model Formulation

A detailed understanding of the transmission of the hepatitis B virus and other emerging pathogens is crucial in its containment, Goldstein *et. al.* (2005). Mathematical models can give insight into potential impact interventions, Hou *et. al.* (2005). The complex interaction of different infection control strategies and their likely impact on transmission can be predicted using mathematical models, Wang *et. al.* (2004). We propose a mathematical model to understand the transmission dynamics and prevalence of HBV. The model is constructed based on the characteristics of HBV transmission and the model of Lan *et. al.* (2010). Note that Lan *et. al.* (2010) considered only six epidemiological groups and did not distinguish the infective class into subgroups. It is observed that the immunity after recovery is lifetime, while the vaccination might wane after sometimes, Edmund *et. al.* (1996). Therefore, we divide the host population into seven epidemiological groups: the proportion susceptible to infection S ; those latently infected E ; uneducated acute infections I_u ; educated acute infections I_e ; carriers C ; recovered R ; and vaccinated V .

$$\frac{dS}{dt} = \mu\omega(1-\nu C) + \psi V - (\mu_0 + \lambda + \varepsilon\beta C + \gamma_3)S \quad (2.1)$$

$$\frac{dE}{dt} = (\lambda + \varepsilon\beta C)S - (\mu_0 + \sigma)E \quad (2.2)$$

$$\frac{dI_u}{dt} = \sigma E - (\mu_0 + 2\gamma_0)I_u \quad (2.3)$$

$$\frac{dI_e}{dt} = \gamma_0 I_u - (\mu_0 + \gamma_1)I_e \quad (2.4)$$

$$\frac{dC}{dt} = \mu\omega\nu C + q(\gamma_0 I_u + \gamma_1 I_e) - (\mu_0 + \mu_1 + \gamma_2)C \quad (2.5)$$

$$\frac{dR}{dt} = \gamma_2 C + (1-q)(\gamma_0 I_u + \gamma_1 I_e) - \mu_0 R \quad (2.6)$$

$$\frac{dV}{dt} = \mu(1-\omega) + \gamma_3 S - (\mu_0 + \psi)V \quad (2.7)$$

$$\text{where, } \lambda = \beta \left(\frac{I_u}{1 + \alpha_1 I_u} + \frac{\eta I_e}{1 + \alpha_2 I_e} \right). \quad (2.8)$$

In this model, the Holling-type II incidence function given by:

$$g(I) = \frac{\beta I}{1 + \omega I}.$$

The choice of this incidence function is necessary due to the preventive measure (and behavioral changes) taken by the susceptible individuals in response to the severity of the disease.

Table 1: The parameters used are defined below

Parameter	Interpretation	Value	Reference
μ	birth rate	0.0121	MOHC (2009)
μ_0	Natural mortality rate	0.00693	MOHC (2009)
μ_1	HBV related mortality rate	0.007	MMWR(2007)
β	Transmission coefficient or effective contact rate	0.00131	Sirajo <i>et.al.</i> (2013)
ψ	Rate of waning of vaccine-induced immunity	0.04	Sirajo <i>et.al.</i> (2013)
Q	Average probability an individual fail to clear an acute infection and develops to carrier state	0.885	Hahnea <i>et. al.</i> (2004)
γ_0	Rate of movement from uncounsel acute to carrier	4 per year	Edmund <i>et. al.</i> (1996)
γ_1	Rate of movement from counsel acute to carrier	2 per year	Edmund <i>et. al.</i> (1996)
γ_2	Rate of movement from carrier to immune	0.025 per year	Edmund <i>et. al.</i> (1996)
γ_3	vaccination rate of susceptible	0 - 100 percent	Lan <i>et.al.</i> (2010)
γ_4	Rate of movement from uncounsel acute to counsel acute	hypothetical	Lan <i>et.al.</i> (2010)
η	Modification Parameter that suggest reduce sexual transmission rate by chronic individual	hypothetical	Lan <i>et.al.</i> (2010)
V	Proportion of perinatal infected HBV positive birth	0.11	Edmund <i>et. al.</i> (1996)
σ	Rate of movement from latent to acute	6 per year	Edmund <i>et.al.</i> (1996)
ε	Reduced transmission rate	0.16	Edmund <i>et.al.</i> (1996)
ψ	Rate of waning of vaccine-induced immunity	0.04	Sirajo <i>et.al.</i> (2013)

The total population $N(t)$ can be obtained from the above models as:

$$N(t) = S(t) + E(t) + I_u(t) + I_e(t) + C(t) + R(t) + V(t) \quad (2.9)$$

$$\frac{dN}{dt} = \mu - \mu_0 N - \mu_1 C \quad (2.10)$$

Here, it is important to note that in the absence of the disease $N(t) \rightarrow \frac{\pi}{\mu_0}$, the dynamics described by the above systems of equations with the region

$$\Omega = \left\{ x = (S, E, I_u, I_e, C, R, V, N) \in \mathbb{R}_+^7 \mid S > 0, E \geq 0, I_u \geq 0, I_e \geq 0, C \geq 0, R \geq 0, V \geq 0, N \leq \frac{\mu}{\mu_0} \right\} \quad (2.11)$$

is positively invariant. Hence the system is both mathematically and epidemiologically well-posed. Therefore, for initial starting point $x \in \mathbb{R}_+^7$, the trajectory lies in Ω . Thus, we restrict our analysis to the region Ω . (where the models make biological sense).

Lemma 1: All the solution of equations 2.1 -2.7 are positive for all $t \geq 0$ provided that the initial conditions are positive.

Proof: Let $\{(S(0), E(0), I_u(0), I_e(0), C(0), R(0), V(0)) \geq 0\} \in \mathbb{R}_+^7$

$$\frac{dS}{dt} = \mu\omega(1 - \nu C) + \psi V - (\lambda + \mu_0 + \varepsilon\beta C + \gamma_3)S(t) \quad (2.12)$$

$$\geq -(\lambda + \mu_0 + \varepsilon\beta C + \gamma_3)S(t) \quad (2.13)$$

This implies that $S'(t) \geq -(\lambda + \mu_0 + \varepsilon\beta C + \gamma_3)S(t)$, by integrating $S'(t)$, we have

$$S(t) \geq S(0)e^{-\int(\lambda + \varepsilon\beta C)dt - (\mu_0 + \gamma_3)t} \geq 0 \quad (2.14)$$

Similarly, it can be shown that $S > 0, E \geq 0, I_u \geq 0, I_e \geq 0, C \geq 0, V \geq 0, R \geq 0$, for all $t > 0$. Hence, all the solutions of HBV model remain positive for all non-negative initial conditions.

Basic Reproduction Number (Graph-Theoretic Method)

A graph-theoretic method for calculating R_0 was discussed extensively in [Tomas and Lewis (2007) and Tomas *et. al.* (2009)]. From the definition of $R_0 = \rho(FV^{-1})$, they are able to derive a series of rules for reducing the digraph associated with $F\lambda^{-1} - V$ to a digraph with zero weight, from which $\lambda = R_0$ is given. The rules are as follows: Rule 1. To reduce the loop $-a_{ii} < 0$ to -1 at node i , every arc entering i has weight divided by a_{ii} ; and Rule 2. For a trivial node i on a path $j \rightarrow i \rightarrow k$, the two arcs are replaced by $j \rightarrow k$ with weight equal to the product.

Using Graph Theoretic Method

Taking the infective classes of the model:

$$\begin{aligned}\frac{dE}{dt} &= (\lambda + \epsilon\beta C)S - (\mu_0 + \sigma)E \\ \frac{dI_u}{dt} &= \sigma E - (\mu_0 + 2\gamma_0)I_u \\ \frac{dI_e}{dt} &= \gamma_0 I_u - (\mu_0 + \gamma_1)I_e \\ \frac{dC}{dt} &= \mu\omega\nu C + q(\gamma_0 I_u + \gamma_1 I_e) - (\mu_0 + \mu_1 + \gamma_2)C\end{aligned}$$

We have four infected classes in this model, those latently infected E , uncounsel acute infections I_u , counsel acute infections I_e , and carriers C , hence our $m = 4$.

$$F = \begin{bmatrix} (\lambda + \epsilon\beta C)S \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad V = \begin{bmatrix} (\mu_0 + 2\sigma)I_u - \sigma E \\ (\mu_0 + \gamma_0 + \gamma_4)I_u - \sigma E \\ (\mu_0 + \gamma_1)I_e - \gamma_4 I_u \\ (\mu_0 + \mu_1 + \gamma_2 + k_3 - \mu\omega\nu)C - q(\gamma_1 I_e + \gamma_0 I_u) \end{bmatrix} \quad (3)$$

Tomas *et.al.* (2009)

$$F = \begin{bmatrix} 0 & \beta S & \eta\beta S & \epsilon\beta S \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad (3.16)$$

$$V = \begin{bmatrix} \mu_0 + \sigma & 0 & 0 & 0 \\ -\sigma & \mu_0 + \gamma_0 + \gamma_4 & 0 & 0 \\ 0 & -\gamma_4 & \mu_0 + \gamma_1 & 0 \\ 0 & -q\gamma_0 & -q\gamma_1 & -\mu\omega\nu + \mu_0 + \mu_1 + \gamma_2 + k_3 \end{bmatrix} \quad (3.17)$$

the above becomes

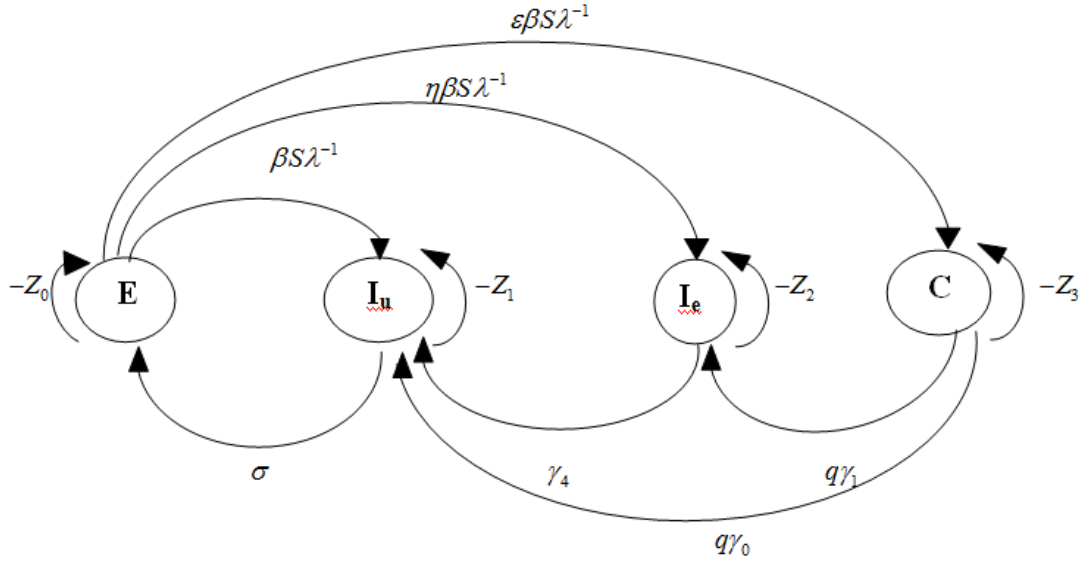
$$V = \begin{bmatrix} Z_0 & 0 & 0 & 0 \\ -\sigma & Z_1 & 0 & 0 \\ 0 & -\gamma_4 & Z_2 & 0 \\ 0 & -q\gamma_0 & -q\gamma_1 & Z_3 \end{bmatrix} \quad (3.18)$$

For the disease free equilibrium point of the system of equations, we have:

$$S_0 = \frac{\mu(\psi + \mu_0\omega)}{\mu_0(\mu_0 + \psi + \gamma_3)}, \quad V_0 = \frac{\mu(\mu_0 + \gamma_3 - \mu_0\omega)}{\mu_0(\mu_0 + \psi + \gamma_3)}$$

$$F\lambda^{-1} - V = \begin{bmatrix} -Z_0 & \beta S\lambda^{-1} & \eta\beta S\lambda^{-1} & \epsilon\beta S\lambda^{-1} \\ \sigma & -Z_1 & 0 & 0 \\ 0 & \gamma_4 & -Z_2 & 0 \\ 0 & q\gamma_0 & q\gamma_1 & -Z_3 \end{bmatrix} \quad (3.19)$$

Creating A Digraph $F\lambda^{-1} - V$



Creating A Trivial Node

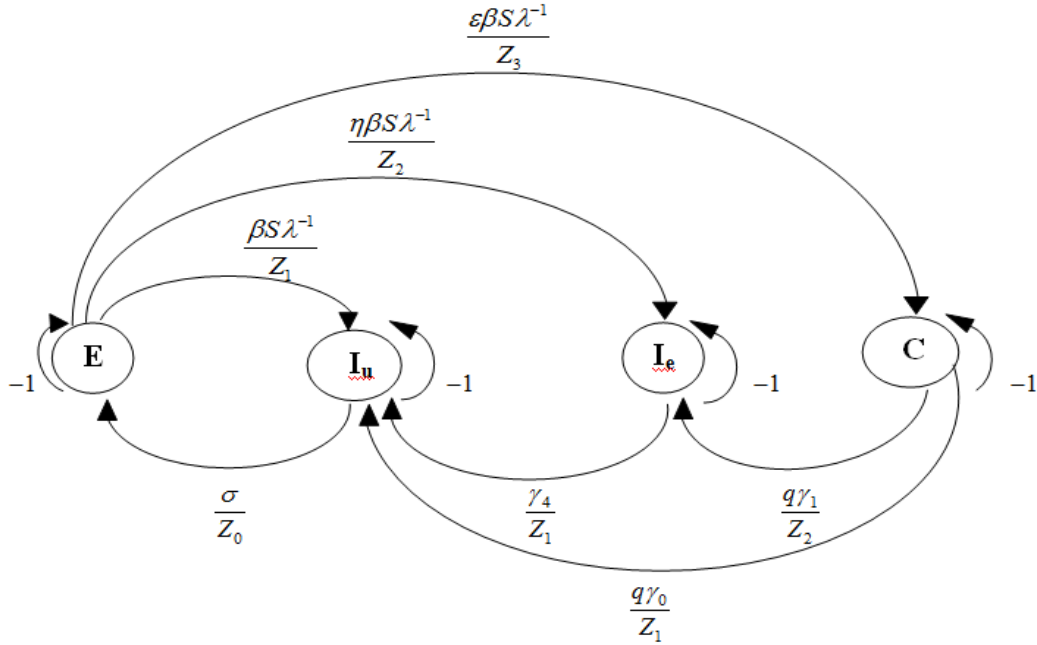


Figure 2: A Digraph and A Trivial Node

Equating the left hand-side to zero, we have:

$$\frac{\eta\gamma_4\beta S\sigma\lambda^{-1}}{Z_2Z_1Z_0} + \frac{\beta S\sigma\lambda^{-1}}{Z_1Z_0} + \frac{\varepsilon\beta S\gamma_1\gamma_4\sigma\lambda^{-1}}{Z_2Z_1Z_0Z_3} + \frac{\varepsilon\beta Sq\gamma_0\sigma\lambda^{-1}}{Z_1Z_0Z_3} = 1 \quad (3.20)$$

$$R_0 = \frac{\beta S\sigma(Z_3(Z_2 + \eta\gamma_4) + \varepsilon q(\gamma_1\gamma_4 + Z_2\gamma_0))}{Z_2Z_1Z_0Z_3} \quad (3.21)$$

Numerical Simulation

We simulated numerically with the aid of Maple 18 Software (2014) to check and determine the effect and behavior of the parameters of the models. The parameters used are obtained from literature, listed in Table 1.

Table 2: Basic Reproduction Number (R_0) obtained for HBV model

Parameters				Basic Reproduction Number (R_0)	
β	γ_3	γ_2	ω	DFE	Remark
1.0	0.05	0.0 Tomas de-Camino-Beck, Mark A. Lewis and P. Van den Driessche (2009)	1.0	71.28492447	Unstable
0.9	0. Tomas de-Camino-Beck, Mark A. Lewis and P. Van den Driessche (2009)	0.025	0.9	27.36520548	Unstable
0.8	0.25	0.035	0.8	13.52206884	Unstable
0.7	0.35	0.045	0.7	7.559082355	Unstable
0.6	0.45	0.055	0.6	4.512072547	Unstable
0.5	0.55	0.065	0.5	2.776925099	Unstable
0.4	0.65	0.075	0.4	1.712 Tomas de-	Unstable

				Camino-Beck, Mark A. Lewis and P. Van den Driessche (2009)2596	
0.3	0.75	0.085	0.3	1.0222294 Tomas de-Camino-Beck, Mark A. Lewis and P. Van den Driessche (2009)	Unstable
0.2	0.85	0.095	0.2	0.5564617425	Stable
0.1	0.95	0.105	0.1	0.2318857139	Stable

Discussion of Results

Simulations illustrate the asymptotic stability of DFE studied in section 3. The model described by equations (2.1 - 2.7) exhibit a rich dynamic. We observed that the biological basic reproduction number R_0 is fundamental for the study of the basic dynamical properties. Applied to hepatitis B, the model suggests that infection rates play a great role in the description of the disease. Simulations conducted confirm our results and suggested the possible ways to curb the outbreak of the disease epidemic. To control HBV infection, we would like to see what parameters can reduce the basic reproduction number. From Table 2, we see that as β (effective contact rate) decreases, R_0 decreases. Consequently, R_0 decreases as $1 - \omega$, γ_2 and γ_3 increase in the model. Therefore, we observed that the immunization of both newborn carrier and susceptible individuals is an efficient intervention.

Conclusion

The use of the spectral radius of the next generation matrix to calculate the basic reproduction number R_0 , is often used in literature. However, at times, this calculation might involve several matrix operations that can be computationally complicated as the number of compartments in the model increases. The graph-theoretic method we presented here allows us to calculate R_0 more easily for some complex epidemiological models. For more complicated systems, the graph-theoretic method might be simpler to apply since the matrix $F\lambda^{-1} - V$ has sparse structure, which avoids the dilemma associated with picking the dominant eigen-value from the matrix. In addition, the model simulations exhibit the challenges of chronic HBV infection: the existence of the exposed class, which is not part of the treatment program is a factor militating against the unstable nature of the model, however, increasing public awareness of carrier and testing of individuals will also have a greater impact alongside the increase in vaccination rate of the population.

Competing interests: The manuscript was read and approved by all the authors. They therefore declare that there is no Conflict of Interest.

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