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A Graph-Theoretic Method for the Basic Reproduction Number in Age-Structured Hepatitis B Model

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ABSTRACT

In this paper, we present an Age-Structured hepatitis B model. This epidemic model is investigated for different classes of infectious diseases that can be transmitted through an effective contact with infective individuals, who are contagious. The Graph-Theoretic Method for the Basic Reproduction Number was obtained. In addition, the numerical simulation is used to virtually verify the model predictions. The result suggest that the endemic nature of the model is approaching equilibrium with increase immunization program and other control measures put in place.

1. Introduction

In the last two decades, mathematical models have frequently been used to study the transmission dynamics of HBV in several regions. Anderson and May [1] used a deterministic, compartmental mathematical model to illustrate the influences of carriers on the transmission of Hepatitis B virus (HBV). Anderson et al. [2] and Williams et al. [3] described models of the sexual transmission of HBV, which include heterogeneous mixing age and sexual activity. Edmunds et al. [4] illustrated the relation between the age at infection with HBV and the development of the carrier state. In 2007, Stanca et al. [5] modeled the mechanisms of acute hepatitis B virus infection, they discovered that a cell-mediated immune response plays a significant role in controlling the virus. Thornley et al. [6] applied the model of Medley et al. [7] to predict chronic hepatitis B infection in New Zealand. Hepatitis B is a severe liver disease caused by the hepatitis B virus (HBV), Edmund et al. [4]. It is a primary global health problem and the most severe type of viral hepatitis. Formerly known as ”serum hepatitis,” the infection has caused epidemics in parts of Africa and Asia; moreover, it is endemic in China, Williams, [8].

2. Mathematical Model Formulation

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 Sirajo et al. [9].The model comprises of nine compartments, here we see the need of treatment of carrier above 15 years of age, because of the need to procure a therapeutic treatment for the

infected individuals in the population. Susceptible individual below 15 years of age ($S_U(t)$), Susceptible individual 15 years and above ($S_F(t)$), Vaccinated V, Infectious individual below 15 years of age ($I_U(t)$), Infectious individual 15 years and above ($I_F(t)$), Chronically infected individual below 15 years of age ($C_U(t)$), Chronically infected individual above 15 years of age ($C_F(t)$), Treatment of chronically infected individual above 15 years of age and above ($T_F(t)$), Recovered (R(t)), and Vaccinated (V(t)). The following assumptions were made: There exist disease induced deaths due to chronic (via single and dually HBV/HIV co-infections). Treatment should be for a long time and uninterrupted, as virological relapses after discontinuation of treatment are frequent. Wanning of HBV vaccination takes 25 years, and it has not been established to be life-long.

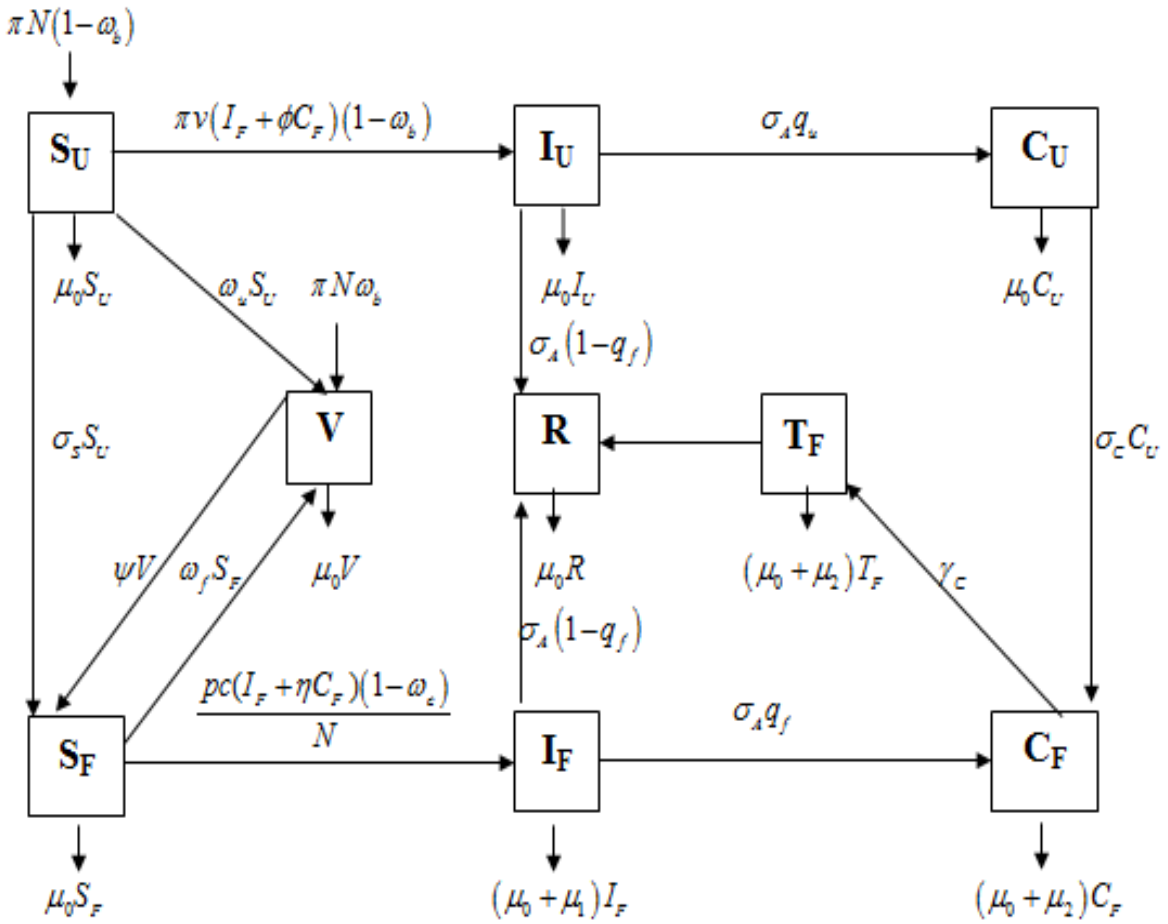


Figure 1: Schematic representation of interactions of HBV transmission

$$\frac{dS_U}{dt} = \pi N\left(1-\omega_b\right) - \pi\nu\left(I_F + \phi C_F\right)\left(1-\omega_b\right)S_U - \left(\sigma_s + \omega_u + \mu_0\right)S_U \tag{1}$$

$$\frac{dS_F}{dt} = \sigma_s S_U + \psi V - \frac{pc\left(I_F + \eta C_F\right)\left(1-\omega_c\right)}{N}S_F - \left(\omega_f + \mu_0\right)S_F \tag{2}$$

$$\frac{dV}{dt} = \pi N\omega_b + \omega_u S_U + \omega_f S_F - \left(\mu_0 + \psi\right)V \tag{3}$$

$$\frac{dI_U}{dt} = \pi\nu\left(I_F + \phi C_F\right)\left(1-\omega_b\right)S_U - \left(\sigma_A + \mu_0\right)I_U \tag{4}$$

$$\frac{dI_F}{dt} = \frac{pc\left(I_F + \eta C_F\right)\left(1-\omega_c\right)}{N}S_F - \left(\mu_0 + \mu_1 + \sigma_A\right)I_F \tag{5}$$

$$\frac{dC_U}{dt} = \sigma_A q_u I_U - \left(\sigma_C + \mu_0\right)C_U \tag{6}$$

$$\frac{dC_F}{dt} = \sigma_A q_f I_F + \sigma_C C_U - \left(\mu_0 + \mu_2 + \gamma_c\right)C_F \tag{7}$$

$$\frac{dT_F}{dt} = \gamma_c C_F - \left(\mu_0 + \mu_2 + \gamma_T\right)T_F \tag{8}$$

$$\frac{dR}{dt} = \sigma_A\left(1-q_u\right)I_U + \sigma_A\left(1-q_f\right)I_F + \gamma_T T_F - \mu_0 R \tag{9}$$

Where,

$\omega_u = \varepsilon_p\tau_u,\ \omega_b = \varepsilon_p\tau_b,\ \omega_f = \varepsilon_p\tau_f, \omega_c = \varepsilon_c\tau_c, \pi_A = \pi\nu\left(1-\omega_b\right), \pi_C = \pi\nu\phi\left(1-\omega_b\right), \beta_A = pc\left(1-\omega_b\right),$

$\beta_C = pc\eta\left(1-\omega_c\right), \gamma_{AU} = \sigma_A\left(1-q_u\right), \gamma_{AF} = \sigma_A\left(1-q_f\right), Z_0 = \mu_0 + \sigma_A, Z_1 = \mu_0 + \sigma_s + \omega_u, Z_2 = \mu_0 + \omega_f,$

$Z_3 = \mu_0 + \psi, Z_4 = \mu_0 + \mu_1 + \sigma_A, Z_5 = \mu_0 + \sigma_C, Z_6 = \mu_0 + \mu_2 + \gamma_C, Z_7 = \mu_0 + \mu_2 + \gamma_T,$

Table 1: The list of parameters / notations

Parameter	Interpretation	Value	Reference
μ	birth rate	0.0121	[11]
μ_0	Natural mortality rate	0.00693	[11]
μ_1	HBV related mortality rate by I U and I F	0.007	[10]
μ_2	HBV related mortality rate by C F and T F	0.00131	[9]
ψ	Rate of waning of vaccine-induced immunity	0.04	[9]
q	Average probability an individual fail to clear an acute infection and develops to carrier state	0.885	[9]
π	birth rate	0.036	[9]
C	Average number of sexual partner	3.233	[9]
P	HBV-Sexual transmission risk rate and pc is the effective contact rate	0.6	[9]
η	Modification Parameter that suggest reduce sexual transmission rate by chronic individual	0.667	[9]
ε_c	Condom efficacy	0.8	[9]
ε_p	Vaccine efficacy	0.9	[9]
v	Proportion of perinatal infected HBV positive birth	0.724	[9]
ϕ	Modification Parameter that suggest reduction in HBV-positive birth by chronic individual	0.159	[9]

σ_s	Rate of moving from S U to S F	0.0667	[9]
σ_A	Rate of moving from acute to chronic infection	2.667	[9]
σ_C	Rate of moving from C U to C F	0.069	[9]
γ_T	Rate of moving from T F to R		Hypothetical
γ_C	Rate of moving from C F to T F	0.015	[9]
q_u	Proportion of I U which progress to C U	0.885	[12]
q_f	Proportion of I F which progress to C F	0.1	[9]
$\tau_c, \tau_b, \tau_u, \tau_f$	Condom, Vaccine(birth), Vaccine (below 15), Vaccine(above 15), compliance	0.1	[9]

The total population N(t) can be obtained from

$$N(t) = S_U(t) + S_F(t) + V(t) + I_U(t) + I_F(t) + C_U(t) + C_F(t) + T_F(t) + R(t)$$

$$\frac{dN}{dt} = \pi N - \mu_0 N - \mu_2 (C_F + T_F)$$

$$N(t) = N(0) e^{(\pi - \mu_0)t} \tag{10}$$

in the absence of disease $N(t) \to \frac{\pi}{\mu_0}$, Moreover, under the dynamics described by the above systems of equations, the region

$$\Omega = \left\{ \begin{array}{l} x = (S_U, S_F, V, I_U, I_F, C_U, C_F, T_F, N) \in \Re_+^9 \mid S_U > 0, S_F > 0, V \geq 0, I_U \geq 0, I_F \geq 0, C_U \geq 0, \\ C_F \geq 0, T_F \geq 0, N \leq \frac{\mu}{\mu_0} \end{array} \right\} \tag{11}$$

is positively invariant. Hence the system is both mathematically and epidemiologically well-posed. Therefore, for initial starting point $x \in \Re_+^9$, the trajectory lies in Ω. Thus we restrict our analysis to the region Ω. (where the models make biological sense)

2.1 Positivity of Solutions

Lemma 1: All the solution of the Equations 1 - 9 are positive for all time t ≥ 0 provided the initial condition are positive.

Proof: Let $\left\{ (S_U(0), S_F(0), V(0), I_U(0), I_F(0), C_U(0), C_F(0), T_F(0), R(0)) \geq 0 \right\} \in \Re_+^9$

$$\frac{dS_U}{dt} = \pi N (1 - \omega_b) - \pi \nu (I_F + \phi C_F)(1 - \omega_b) S_U - (\sigma_s + \omega_u + \mu_0) S_U \tag{12}$$

$$\geq -\pi \nu (I_F + \phi C_F)(1 - \omega_b) S_U - (\sigma_s + \omega_u + \mu_0) S_U \tag{13}$$

This implies $S_U'(t) \geq -\pi \nu (I_F + \phi C_F)(1 - \omega_b) S_U - (\sigma_s + \omega_u + \mu_0) S_U$, integrating we have

$$S_U(t) \geq S_U(0) e^{-\pi \nu (1 - \omega_b) \int (I_F + \phi C_F) dt - (\sigma_s + \omega_u + \mu_0) t} \geq 0 \tag{14}$$

similarly it can be shown that $S_U > 0, S_F > 0, V \geq 0, I_U \geq 0, I_F \geq 0, C_U \geq 0, C_F \geq 0, T_F \geq 0, R \geq 0$, for all time t > 0. Hence all solutions of the HBV model remain positive for all non-negative initial conditions.

3. Basic reproduction number (Graphic-Theroretic Method)

A graph-theoretic method for calculating R_0 was discussed exclusively in Tomas et al.[13], [14]. 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} .

Rule 2. For a trivial node i on a path j → i → k, the two arcs are replaced by j → k with weight equal to the product.

Using Graph Theoretic Method

Taking the infective classes of the model;

$$\frac{dI_U}{dt} = \pi\nu\left(I_F + \phi C_F\right)\left(1-\omega_b\right)S_U - \left(\sigma_A + \mu_0\right)I_U$$

$$\frac{dI_F}{dt} = \frac{pc\left(I_F + \eta C_F\right)\left(1-\omega_c\right)}{N}S_F - \left(\mu_0 + \mu_1 + \sigma_A\right)I_F$$

$$\frac{dC_U}{dt} = \sigma_A q_u I_U - \left(\sigma_C + \mu_0\right)C_U$$

$$\frac{dC_F}{dt} = \sigma_A q_f I_F + \sigma_C C_U - \left(\mu_0 + \mu_2 + \gamma_c\right)C_F$$

We have four infected classes in this model, Infectious individual below 15 years of age ($I_U(t)$), Infectious individual 15 years and above ($I_F(t)$), Chronically infected individual below 15 years of age ($C_U(t)$), Chronically infected individual 15 years and above ($C_F(t)$), hence our m = 4.

$$F = \begin{bmatrix} 0 \\ \left(\beta_A I_F + \beta_C C_F\right)S_F \\ 0 \\ 0 \end{bmatrix}, \qquad V = \begin{bmatrix} Z_0 I_U - \pi_A I_F S_U - \pi_C C_F S_U \\ Z_4 I_U \\ Z_5 C_U - \sigma_A q_u I_U \\ Z_6 C_F - \sigma_A q_f I_F - \sigma_C C_U \end{bmatrix} \tag{15}$$

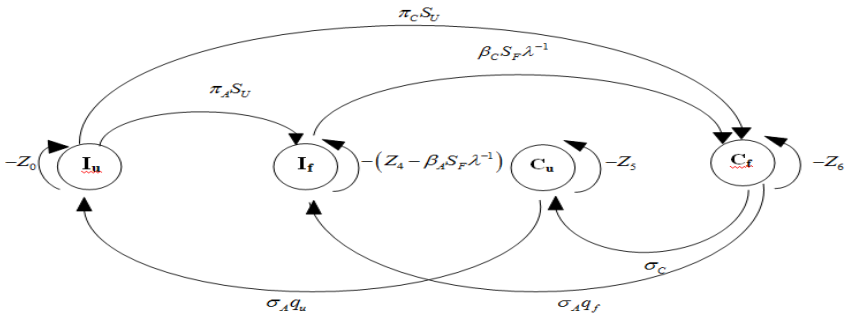
$$F = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & \beta_A S_F & 0 & \beta_C S_F \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \qquad (16) \qquad V = \begin{bmatrix} Z_0 & \pi_A S_U & 0 & \pi_C S_U \\ 0 & Z_4 & 0 & 0 \\ -\sigma_A q_u & 0 & Z_5 & 0 \\ 0 & -\sigma_A q_f & -\sigma_C & Z_6 \end{bmatrix} \tag{17}$$

For the disease free equilibrium point of the system of equations, which has the coordinates:

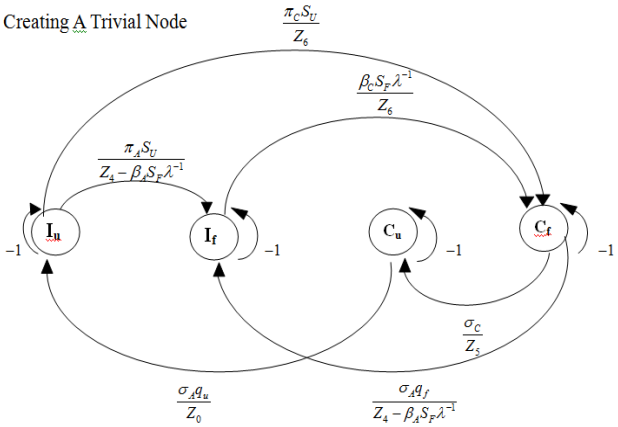
$$S_U^* = \frac{\pi N\left(1-\omega_b\right)}{Z_1}, \qquad S_F^* = \frac{Z_4\left(-q_u\pi_c\sigma_A\sigma_C + Z_6 Z_5 Z_4\right)}{\pi_A q_u \beta_c \sigma_A \sigma_C - \pi_C q_u \beta_A \sigma_A \sigma_C + Z_4 Z_5 q_f \beta_C \sigma_A + \beta_A Z_6 Z_5 Z_4}$$

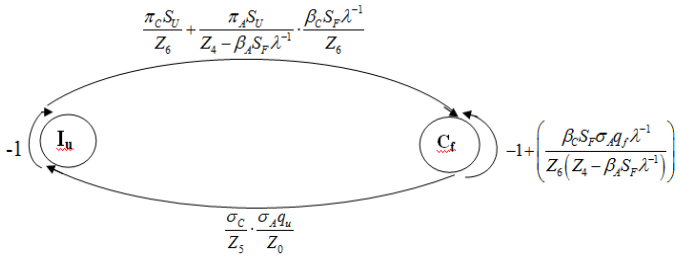
$$F\lambda^{-1}-V=\begin{bmatrix} -Z_0 & \pi_A S_U & 0 & \pi_C S_U \\ 0 & \beta_A S_F \lambda^{-1}-Z_4 & 0 & \beta_C S_F \lambda^{-1} \\ \sigma_A q_u & 0 & -Z_5 & 0 \\ 0 & \sigma_A q_f & \sigma_C & -Z_6 \end{bmatrix} \tag{18}$$

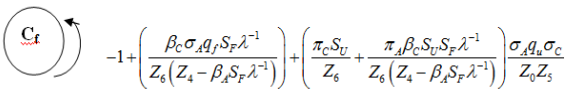
Creating A Digraph $F\lambda^{-1}-V$



Creating A Trivial Node







equating the left hand-side to zero, we have;

$$\frac{\beta_C \sigma_A S_F\left(\pi_A S_U q_u \sigma_C + Z_5 Z_0 q_f\right)}{Z_6 \lambda\left(-\beta_A S_F + Z_4\right) Z_5 Z_0} + \frac{\sigma_C \sigma_A q_u \pi_C S_U}{Z_6 Z_5 Z_0} = 1 \tag{19}$$

$$R_0 = \lambda = \frac{S_F\left(\left(S_U q_u\left(-\pi_A \beta_C + \pi_C \beta_A\right)\sigma_C - \beta_C Z_5 Z_0 q_f\right)\sigma_A - \beta_A Z_6 Z_5 Z_0\right)}{Z_4\left(\pi_C \sigma_C \sigma_A q_u S_U - Z_6 Z_5 Z_0\right)} \tag{20}$$

4. Results and Discussion

We simulated numerically with the aid of Maple 18 software [15] to check and determine the effect and behavior of the parameters of the model. This illustrate the asymptotic stability of Disease free equilibrium (DFE) of the model. The model described by Equations (1 - 9) exhibit a rich dynamic. We observed that varying these control parameters; τ_b, τ_u, τ_c, τ_f, when there is no control (effective immunization's and condom usage equal zero) our R_0 = 2.9479, at low rate (10 percent) R_0 = 1.6145, at moderate rate (50 percent) R_0 = 0.3823, at high rate (90 percent) R_0 = 0.0987. However, the table below also show the gradual decrease in the reproduction number when different control measures put in place are increased. The result established here is more effective in bringing the basic reproduction number below unity, when compared with the results from literature owing to the treatment class adopted.

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

Parameter	$R_0^{\tau_b}$		$R_0^{\tau_u}$		$R_0^{\tau_c}$		$R_0^{\tau_f}$	
τ_b, τ_u, τ_c, τ_f	DFE	Remark	DFE	Remark	DFE	Remark	DFE	Remark
0.1	0.4664	Stable	0.3767	Stable	0.6115	Stable	1.2621	Unstable
0.2	0.4454	Stable	0.3795	Stable	0.5752	Stable	0.8847	Stable
0.3	0.4244	Stable	0.3809	Stable	0.5389	Stable	0.6811	Stable
0.4	0.4033	Stable	0.3817	Stable	0.5026	Stable	0.5536	Stable
0.5	0.3823	Stable	0.3822	Stable	0.4663	Stable	0.4664	Stable
0.6	0.3612	Stable	0.3827	Stable	0.4301	Stable	0.4029	Stable
0.7	0.3400	Stable	0.3830	Stable	0.3938	Stable	0.3546	Stable
0.8	0.3188	Stable	0.3832	Stable	0.3576	Stable	0.3166	Stable
0.9	0.2976	Stable	0.3834	Stable	0.3213	Stable	0.2860	Stable
1.0	0.2763	Stable	0.3835	Stable	0.2850	Stable	0.2608	Stable

5. Conclusion

In conclusion, the results suggests that the more we vaccinate and provide adequate treatment to the population and also enlighten them on its menace, this will bring the threshold value below unity, thus eradicating the disease. Moreover, other highly sensitive parameters are σ_A , σ_C , σ_S ,η, γ_C and $\gamma_{TF.}$ For the parameters σ_A and q_f are the movement from an acute stage to a chronic stage and should be of high sensitivity. The acute stages have short duration (six months) while chronic stages have the long duration of years and in most cases they are life-long. For η, it is the modification parameter that suggests the reduced sexual transmission rate by chronic individuals, and thus, it profoundly affects the transmission dynamics of the disease.

7. Conflict of Interest

There is no conflict of interest associated with this work.

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