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Optimal Control on Hepatitis B Virus Model with Non-Monotonic Incidence Function

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ABSTRACT

In this paper, a time - dependent model of prophylactic vaccination HBV is considered. This epidemic model is being investigated for various infectious diseases classes, counsel and uncounsel. Mathematical analyzes are performed to determine the positivity and we applied an optimal control strategies in the form of vaccination to minimize or eradicate transmission from mother to child. The study concluded that prophylactic vaccination is not an efficient way to curb the epidemic.

1. Introduction

Hepatitis is an inflammation of the liver caused by viruses, bacterial infections, or constant vulnerability to alcohol intake, drugs, or toxic chemicals, such as those obtained in aerosol sprays and paint thinners [1]. Inflammation is the painful, red growth that results when tissues of the body become wounded or infected. Inflammation can cause organs not to work properly. Hepatitis can also result from an autoimmune disorder, in which the body wrongly sends disease-fighting cells to attack its healthy tissue, in this case, the liver [2]. The liver is located in the upper right-hand side of the abdomen, mostly behind the rib cage. The liver of an adult typically weighs close to three pounds [3]. No matter its cause, hepatitis decreases the liver's ability to make life-preserving functions, including filtering fatal infectious agents from the blood, storing blood sugar and converting it to usable energy forms, and producing many proteins necessary for life [4].
World Health Organization [5] has described Hepatitis B as a potentially life-threatening liver infection of global importance. An approximated 240 million people worldwide are chronically affected with this virus, and more than 780,000 people die each year from the complexities associated with Hepatitis B. The infection occurs in two phases. The first is an acute phase, which, in most people, doesn't result in any ill-health symptoms. However, a few people may experience an acute illness lasting several weeks with symptoms including jaundice, extreme fatigue, dark urine, nausea, vomiting and abdominal pain. Fewer still can develop acute liver failure, which can lead to death. The second phase is a chronic carrier state in which the virus remains in the liver and may ultimately cause chronic liver insufficiency, liver cirrhosis or primary liver cell cancer.

These carriers show no overt signs of ill-health, and they are usually the source of all new infections.

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 [6]. Note that they proposed a six compartmental model for the propagation of the epidemic model. It is observed that the immunity after recovery is not lifetime, while the vaccination might wane after some time [7]. Figure 1 show the schematic representation of interactions of HBV transmission. 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 Ie; carriers C; recovered R; and Vaccinated V.

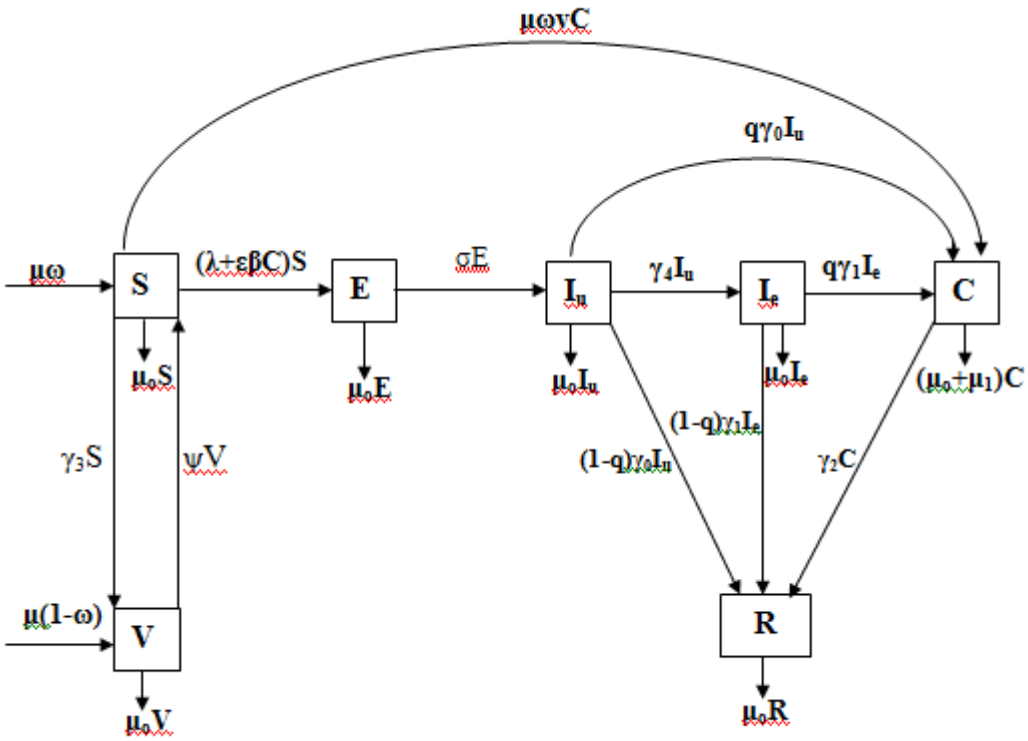

Figure 1: Schematic representation of interactions of HBV transmission

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

$$\frac{dE}{dt} = \left(\lambda+\varepsilon\beta C\right)S-\left(\mu_0+\sigma\right)E \quad (2)$$

$$\frac{dI_u}{dt} = \sigma E-\left(\mu_0+\gamma_0+\gamma_4\right)I_u \quad (3)$$

$$\frac{dI_e}{dt} = \gamma_4 I_u-\left(\mu_0+\gamma_1\right)I_e \quad (4)$$

$$\frac{dC}{dt} = \mu\omega\nu C + q\left(\gamma_0 I_u + \gamma_1 I_e\right) - \left(\mu_0 + \mu_1 + \gamma_2\right)C \quad (5)$$

$$\frac{dR}{dt} = \gamma_2 C + \left(1-q\right)\left(\gamma_0 I_u + \gamma_1 I_e\right) - \mu_0 R \quad (6)$$

$$\frac{dV}{dt} = \mu\left(1-\omega\right) + \gamma_3 S - \left(\mu_0 + \psi\right)V \quad (7)$$

Where, $\lambda = \beta\left(\frac{I_u}{1+\alpha_1 I_u} + \frac{\eta I_e}{1+\alpha_2 I_e}\right)$ (8)

In this model, the Holling-type II incidence function given by $g\left(I\right) = \frac{\beta I}{1+\omega I}$.

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.
The parameters used are defined in Table 1.

Table 1: the parameters of the model are defined in the table below

Parameter	Interpretation	Value	Reference
μ	Birth rate	0.0121	[8]
μ_0	Natural mortality rate	0.00693	[8]
μ_1	HBV related mortality rate	0.007	[9]
β	Transmission coefficient or effective contact rate	0.00131	[8]
ω	Proportion of births without successful vaccination	0 – 100 percent	[6]
q	Average probability an individual fails to clear an acute infection and develops to carrier state	0.885	[10]
γ_0	Rate of movement from uncounsel acute to carrier	4 per year	[7]
γ_1	Rate of movement from counsel acute to carrier	2 per year	[7]
γ_2	Rate of movement from carrier to immune	0.025 per year	[7]
γ_3	Vaccination rate of susceptible	0 - 100 percent	[7]
γ_4	Rate of movement from uncounsel acute to counsel acute	Hypothetical	
σ	Rate of movement from latent to acute	6 per year	[7]
ε	Reduced transmission rate	0.16	[7]
ψ	Rate of waning of vaccine-induced immunity	0.04	[11]
ν	Proportion of prenatally infected (carrier mothers)	0.11	[7]

The total population N (t) can be obtained from

$$N(t) = S\left(t\right) + E\left(t\right) + I_u\left(t\right) + I_e\left(t\right) + C\left(t\right) + R\left(t\right) + V\left(t\right) \quad (9)$$

$$\frac{dN}{dt} = \mu - \mu_0 N - \mu_1 C \quad (10)$$

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

$$\Omega = \left\{ x = (S, E, I_u, I_e, C, R, V, N) \in \Re_+^7 \mid S > 0, E \geq 0, \ I_u \geq 0, I_e \geq 0, C \geq 0, V \geq 0, N \leq \frac{\mu}{\mu_0} \right\} \quad (11)$$

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

Theorem 1 All the solution of the equations (1 – 7) are positive for all time t ≥ 0 provided the initial condition are positive.

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

$$\frac{dS}{dt} = \mu\omega(1 - \nu C) + \psi V - (\lambda + \mu_0 + \varepsilon\beta C + \gamma_3) S(t) \quad (12)$$

$$\geq -(\lambda + \mu_0 + \varepsilon\beta C + \gamma_3) S(t) \quad (13)$$

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

$$S(t) \geq S(0) e^{-\int (\lambda + \varepsilon\beta C) dt - (\mu_0 + \gamma_3) t} \geq 0 \quad (14)$$

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 time t > 0. Hence all solutions of the HBV model remain positive for all non-negative initial conditions.

3. Optimal Model

$$\frac{dS}{dt} = \mu\omega(1 - \nu C + \nu u_1 C) + \psi V - (\mu_0 + \lambda + \varepsilon\beta C + u_2\gamma_3) S \quad (15)$$

$$\frac{dE}{dt} = (\lambda + \varepsilon\beta C) S - (\mu_0 + \sigma) E \quad (16)$$

$$\frac{dI_u}{dt} = \sigma E - (\mu_0 + \gamma_0 + \gamma_4) I_u \quad (17)$$

$$\frac{dI_e}{dt} = \gamma_4 I_u - (\mu_0 + \gamma_1) I_e \quad (18)$$

$$\frac{dC}{dt} = \mu\omega\nu(1 - u_1) C + q(\gamma_0 I_u + \gamma_1 I_e) - (\mu_0 + \mu_1 + \gamma_2) C \quad (19)$$

$$\frac{dR}{dt} = \gamma_2 C + (1 - q)(\gamma_0 I_u + \gamma_1 I_e) - \mu_0 R \quad (20)$$

The problem is to minimize or eradicate completely mother to child transmission and the cost control implication on the vaccination strategies employed. The objective function is given as;

$$J(u_1, u_2) = \int_{t_0}^{t_1} A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) \ dt \quad (21)$$

Where, the rate of professional effort that the medical expatriate put in place in prevention or eradicate of mother to child transmission (u_1) and cost of controlling the vaccination (u_2). The total cost includes not only the consumption for every individual, but also the cost of organization, management, and cooperation, etc. Hence, the coefficients, A_1, A_2, B_1, and B_2, are balancing cost factors due to scales and the importance of the four parts of the objective function above.
Using similar control variables and objective function (as in above) we find that the Hamiltonian takes the form;

$$H = A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) + \sum_{i=1}^{6} \lambda_i f_i \quad (22)$$

Where,

$z_0 = \mu_0 + \sigma, \quad z_1 = \mu_0 + \gamma_0 + \gamma_4, \quad z_2 = \mu_0 + \gamma_1, \quad z_3 = -\mu\omega\nu + \mu_0 + \mu_1 + \gamma_2, \quad z_4 = \mu_0 + \psi.$

$$H = A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) + \lambda_1 \left[\mu\omega(1 - \nu C + \nu u_1 C) + \psi V - (\mu_0 + \lambda + \varepsilon\beta C + \gamma_3 u_2) S \right]$$
$$+ \lambda_2 \left[(\lambda + \varepsilon\beta C) S - Z_0 E \right] + \lambda_3 \left[\sigma E - Z_1 I_u \right] + \lambda_4 \left[\gamma_4 I_u - Z_2 I_e \right] + \lambda_5 \left[\mu\omega\nu(1 - u_1) C + q(\gamma_0 I_u + \gamma 1 I_e) - Z_3 C \right]$$
$$+ \lambda_6 \left[\mu(1 - \omega) + \gamma_3 u_2 S - Z_5 V \right] \quad (23)$$

.

$$\lambda_1' = -A_1 + \lambda_1 \left[\mu_0 + \lambda + \varepsilon\beta C + \gamma_3 u_2 \right] - \left[\lambda + \varepsilon\beta C \right] \lambda_2 - \gamma_3 u_2 \lambda_6 \quad (24)$$

$$\lambda_2' = Z_0 \lambda_2 - \lambda_3 \sigma \quad (25)$$

$$\lambda_3' = \frac{\beta S}{(1 + \alpha_1 I_u)^2} (\lambda_1 - \lambda_2) + Z_1 \lambda_3 - q\gamma_0 \lambda_5 - \gamma_4 \lambda_4 \quad (26)$$

$$\lambda_4' = \frac{\eta\beta S}{(1 + \alpha_2 I_e)^2} (\lambda_1 - \lambda_2) + Z_2 \lambda_4 - q\gamma_1 \lambda_5 \quad (27)$$

$$\lambda_5' = -A_2 + \mu\omega\nu(1 - u_1)(\lambda_5 - \lambda_1) + \mu\omega\nu\lambda_1 - \varepsilon\beta S(\lambda_1 - \lambda_2) + Z_3 \lambda_5 \quad (28)$$

$$\lambda_6' = -\psi\lambda_1 - Z_4 \lambda_6 \quad (29)$$

With transversality conditions $\lambda_i(t_f) = 0$ (i = 1, ..., 6, t_f is the end time). Using the Hamiltonian, we obtain the optimality conditions.

$$u_1 = \frac{(\lambda_5 - \lambda_1) \mu\omega\nu C}{B_1} \quad (30)$$

$$u_2 = \frac{(\lambda_1 - \lambda_7) \gamma_3 S}{B_2} \quad (31)$$

4. Results and Discussion

4.1. Numerical Solution

To obtain further insight into the influence of the control parameters on the behavior of the systems under consideration, thus, we consider the following Figures plotted with the aid of Maple 18 Software [12].

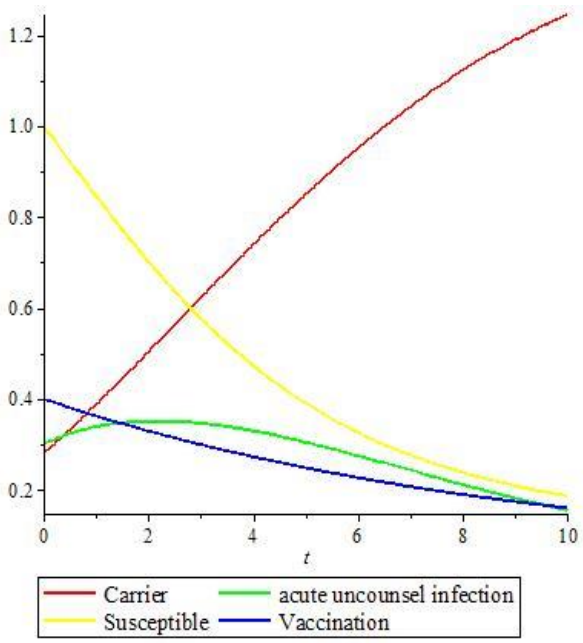

Figure 2: Graph of Carrier, Acute uncounsel infectious, Susceptible and Vaccination at u_1=1,
initial stage (without control)

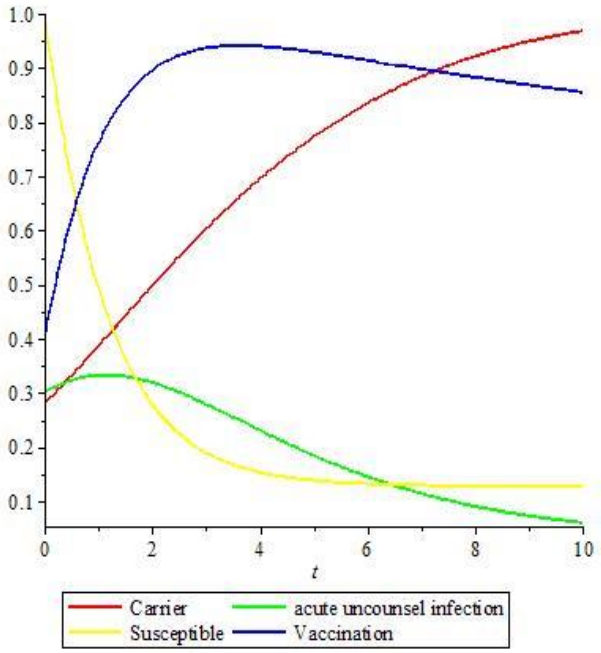

Figure 3: Graph of Carrier, Acute uncounsel infectious, Susceptible and Vaccination at

u_2=0.9

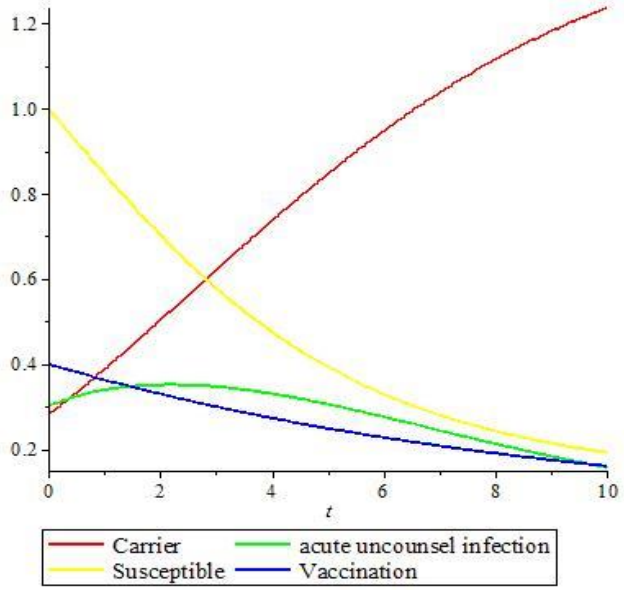

Figure 4: Graph of Carrier, Acute uncounsel infectious, Susceptible and Vaccination at u_1=0.1,

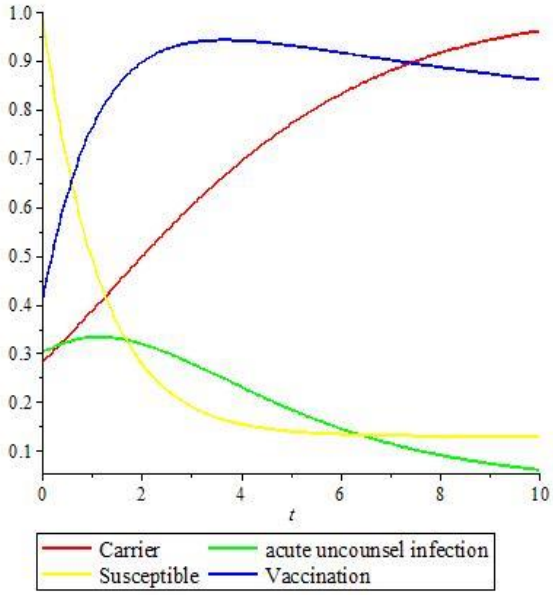

Figure 5: Graph of Carrier, Acute uncounsel infectious, Susceptible and Vaccination at

u_1=0.1, u_2=0

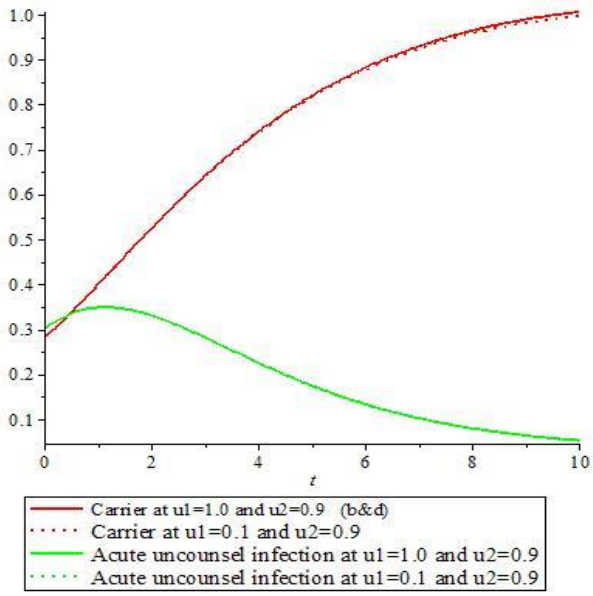

Figure 6: Graph showing the sensitivity in Carrier and Acute uncounsel infectious in figure 2 and 4

u_2=0.9

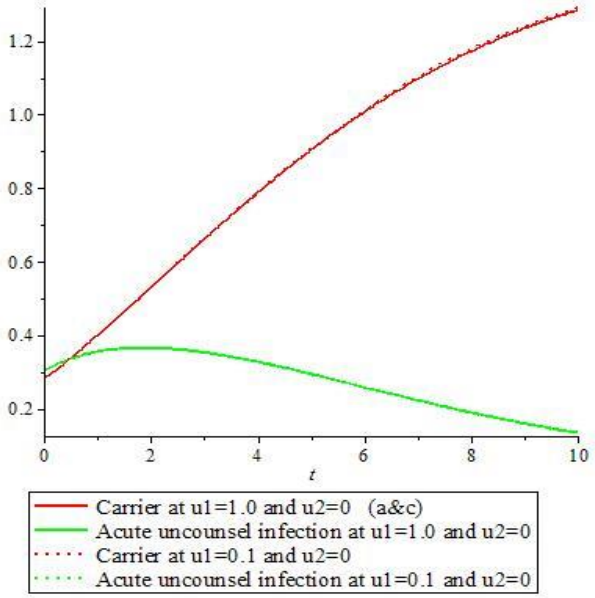

Figure 7: Graph showing the sensitivity in Carrier and Acute uncounsel infectious in figure 3 and 5

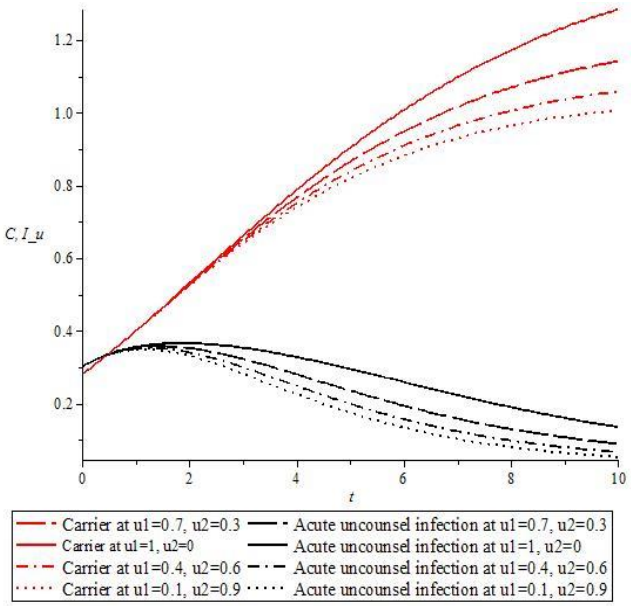

Figure 8: Graph showing the sensitivity in Carrier and Acute uncounsel infectious for different values of control

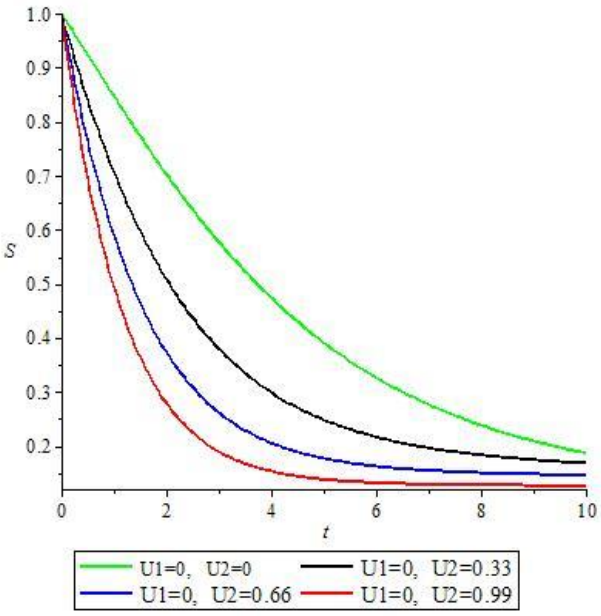

Figure 9: The plot shows the change in Susceptible populations at different values of control

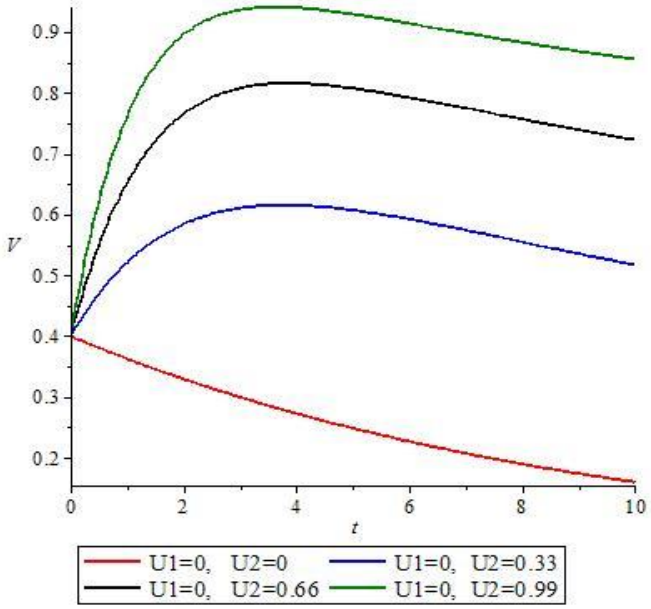

Figure 10: The plot shows the change in Vaccination populations at different values of control

To understand the relationship between the two control parameters (the rate of prevention or eradicates of mother to child transmission u_1 and the cost of controlling the vaccination u_2) in the model, we solved the optimal control problem when $u_1 = 0$ and $u_2 = 0$ (no control) (Figure 2), by setting $u_1 = 1$ and $u_2 = 0.9$ (Figure 3) and looking at the resulting scale for $u_1 = 0.1$ and $u_2 = 0$ (Figure 4) and also considering when $u_1 = 0.1$ and $u_2 = 0.9$ (Figure 5). The four scenarios show two major significant difference, Figure 2 and 4, Figure 3 and 5, respectively, show small difference as portrayed by Figure 6 and 7. We own this change to the control parameter u_1, while the major change (Figure 8) recorded is due to the cost effectiveness of the vaccination strategies u_2. Moreover, we also show the effect of the control parameters on both the Susceptible and Vaccination population in Figure 9 and Figure 10 respectively. This delivers significantly better results due to the split in the acute infectious class into acute counsel and acute uncounsel infectious classes. However, when comparing our results to those of older studies [6], it must be pointed out that the acute class differs and the optimal strategies in transmission and vaccination are better approach in assessing how well the model behaves.

5. Conclusion

In this paper, we proposed seven compartmental models of Hepatitis B virus infection with two controls; the prevention or eradicates of mother to child transmission (u_1) and cost of controlling the vaccination strategies employed (u_2). The positivity of the model is obtained. Thus, we formulate an optimal control problem and solved it using the Pontryagin's maximum principle. The results established shows that effort put in place in subduing or eliminating the birth of carrier by prenatally infected carrier mother is not a sufficient intervention to employ. The study concluded that prophylactic vaccination is not a sufficient way to curb the epidemic.

6. Conflict of Interest

There is no conflict of interest associated with this work.

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