

Optimal Control Approach on Hepatitis B Model with Vaccinations

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Abstract

We present a time-dependent HBV epidemic model with both prophylactic and therapeutic vaccination. This epidemic model is investigated for different classes of infectious diseases. Mathematical analyses are carried out, that determines the positivity of solution and an optimal control approach is applied in order to find the best way to fight the disease. An optimal control strategy in the form of vaccination, and to minimize or eradicate of mother to child transmission, is used. The study concluded that both prophylactic and therapeutic vaccination is an efficient way to curb the epidemic.

Keywords: Vaccination, Optimal control, Epidemic, Time-dependent

Introduction

Inflammation of the liver caused by viruses, bacterial infections, or constant vulnerability to alcohol intake, chemicals, such as those obtained in aerosol sprays and paintthinners [1]. Inflammation is the painful, red results when tissues of the body become wounded or infected. Inflammation can cause organs not to work. Hepatitis can also result from an autoimmune disorder, in which the body wrongly sends disease-fighting cells to liver tissue, in this case, the liver [2]. The liver is located in the upper right-hand side of the abdomen, mostly on the right side. 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, 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 estimated 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 with several weeks with symptoms including jaundice, extreme fatigue, dark urine, nausea, vomiting and abdominal pain. They 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 people show no overt signs of ill-health, and they are usually the source of all new infections.

Mathematical Model Formulation

We propose a mathematical model to understand the transmission dynamics and prevalence of HBV. The model is based on the characteristics of HBV transmission and the model [6]. Note that they proposed a seven compartmental model for the propagation of the epidemic model, a model with multiple transmission of the acute counsel, and carrier infection classes. It is observed that the immunity after recovery is not lifetime, while the immunity wane after some time [7]. Therefore, we divide the host population into eight epidemiological groups: the susceptible to infection S; those latently infected E; uneducated acute infections I_u ; educated acute infections I_E ; recovered or; Treatment T and Vaccinated V.

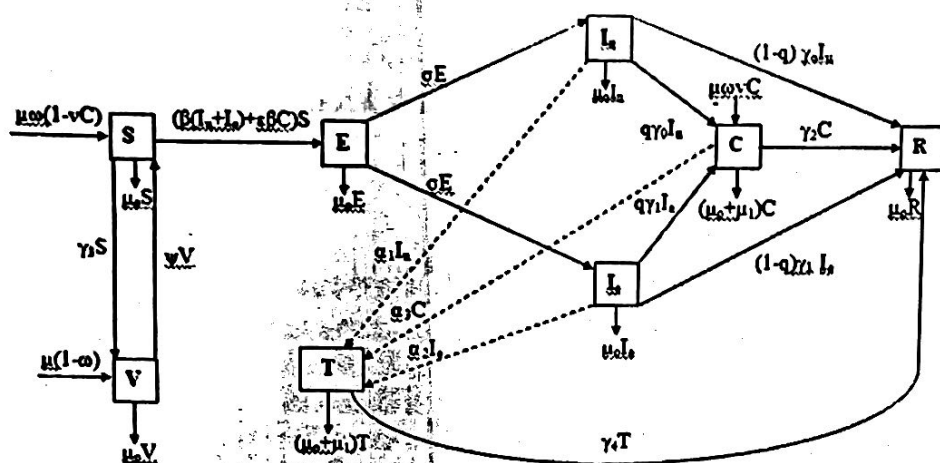


Figure 1: Schematic representation of interactions of HBV transmission

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

$$\frac{dE}{dt} = (\beta(I_u + I_e) + \epsilon\beta C)S - (\mu_0 + 2\sigma)E \quad (2.2)$$

$$\frac{dI_u}{dt} = \sigma E - (\mu_0 + \gamma_0 + \alpha_1)I_u \quad (2.3)$$

$$\frac{dI_e}{dt} = \sigma E - (\mu_0 + \gamma_1 + \alpha_2)I_e \quad (2.4)$$

$$\frac{dC}{dt} = \mu\omega\nu C + q(\gamma_0 I_u + \gamma_1 I_e) - (\mu_0 + \mu_1 + \gamma_2 + \alpha_3)C \quad (2.5)$$

$$\frac{dR}{dt} = \gamma_2 C + \gamma_4 T + (1-q)(\gamma_0 I_u + \gamma_1 I_e) - \mu_0 R \quad (2.6)$$

$$\frac{dT}{dt} = \alpha_1 I_u + \alpha_2 I_e + \alpha_3 C - (\mu_0 + \mu_1 + \gamma_4)T \quad (2.7)$$

$$\frac{dV}{dt} = \mu(1-\omega) + \gamma_3 S - (\mu_0 + \psi)V \quad (2.8)$$

The parameters used are defined in Table 1

Interpretation	Value	Reference
Birth rate	0.0121	[8]
Natural mortality rate	0.00693	[8]
HBV related mortality rate	0.007	[9]
Transmission coefficient or effective contact rate	0.00131	[8]
Proportion of births without successful vaccination	0 – 100 percent	[10]
Average probability an individual fails to clear an acute infection and develops to carrier state	0.885	[11]
Rate of movement from uncounsel acute to carrier	4 per year	[7]
Rate of movement from counsel acute to carrier	2 per year	[7]
Rate of movement from carrier to immune	0.025 per year	[7]
Vaccination rate of susceptible	0 - 100 percent	[7]
Rate of movement from uncounsel acute to counsel acute	Hypothetical	
Rate of therapeutic vaccination/treatment of uncounsel acute individuals	Hypothetical	
Rate of therapeutic vaccination/treatment of counsel acute individuals	Hypothetical	
Rate of therapeutic treatment of chronic carrier individuals	Hypothetical	
Rate of movement from latent to acute	6 per year	[7]
Reduced transmission rate	0.16	[7]
Rate of waning of vaccine-induced immunity	0.04	[12]
Proportion of prenatally infected (carrier mothers)	0.11	[7]

The total population $N(t)$ can be obtained from

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

$$- \mu_0 N - \mu_1 (T + C) \quad (2.10)$$

important to note that in the absence of the disease $N(t) \rightarrow \frac{\mu}{\mu_0}$. Moreover, under the dynamics described by the

systems of equations, the region.

$$\Omega = \{(S, E, I_u, I_e, C, R, T, V, N) \in \mathbb{R}_+^8 \mid S > 0, E \geq 0, I_u \geq 0, I_e \geq 0, C \geq 0, V \geq 0, T \geq 0, N \leq \frac{\mu}{\mu_0}\} \quad (2.11)$$

is positively invariant. Hence the system is both mathematically and epidemiologically well-posed. Therefore, for initial point $x \in \mathbb{R}_+^8$, the trajectory lies in Ω . Thus we restrict our analysis to the region Ω . (Where the models make sense)

All the solution of the equations (2.1 -2.8) are positive for all time $t \geq 0$ provided the initial condition are positive.

$$\{(S(0), E(0), I_u(0), I_e(0), C(0), R(0), T(0), V(0)) \geq 0\} \in \mathbb{R}_+^8$$

$$(-\nu C) + \psi V - (\beta(I_u + I_e) + \mu_0 + \varepsilon\beta C + \gamma_3)S(t) \quad (2.12)$$

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

$S'(t) \geq -(\beta(I_u + I_e) + \mu_0 + \varepsilon\beta C + \gamma_3)S(t)$, integrating we have

$$S(t) \geq S(0)e^{-\int_0^t (\beta(I_u + I_e) + \mu_0 + \varepsilon\beta C + \gamma_3) dt} \geq 0 \quad (2.14)$$

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

3.0 Optimal Control Model

$$\frac{dS}{dt} = \mu\omega(1-vC+vu_1C) + \psi V - (\mu_0 + \beta(I_u + I_e) + \varepsilon\beta C + u_2\gamma_3)S \quad (3.1)$$

$$\frac{dE}{dt} = (\beta(I_u + I_e) + \varepsilon\beta C)S - (\mu_0 + 2\sigma)E \quad (3.2)$$

$$\frac{dI_u}{dt} = \sigma E - (\mu_0 + \gamma_0 + \alpha_1)I_u \quad (3.3)$$

$$\frac{dI_e}{dt} = \sigma E - (\mu_0 + \gamma_1 + \alpha_2)I_e \quad (3.4)$$

$$\frac{dC}{dt} = \mu\omega v(1-u_1)C + q(\gamma_0 I_u + \gamma_1 I_e) - (\mu_0 + \mu_1 + \gamma_2 + \alpha_3)C \quad (3.5)$$

$$\frac{dR}{dt} = \gamma_2 C + \gamma_4 T + (1-q)(\gamma_0 I_u + \gamma_1 I_e) - \mu_0 R \quad (3.6)$$

$$\frac{dT}{dt} = \alpha_1 I_u + \alpha_2 I_e + \alpha_3 C - (\mu_0 + \mu_1 + \gamma_4)T \quad (3.7)$$

$$\frac{dV}{dt} = \mu(1-\omega) + \gamma_3 S - (\mu_0 + \psi)V \quad (3.8)$$

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

$$J(u_1, u_2) = \int_0^t A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) dt$$

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 , C_1 , and C_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;

$$H = A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) + \sum_{i=1}^7 \lambda_i f_i \quad (3.9)$$

Where,

$$z_0 = \mu_0 + 2\sigma, z_1 = \mu_0 + \gamma_0 + \alpha_1, z_2 = \mu_0 + \gamma_1 + \alpha_2, z_3 = -\mu\omega v + \mu_0 + \mu_1 + \gamma_2 + \alpha_3, z_4 = \mu_0 + \mu_1 + \gamma_4, z_5 = \mu_0 + \psi.$$

$$H = A_1 S(t) + A_2 C(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t) + \lambda_1 [\mu\omega(1-vC+vu_1C) + \psi V - (\mu_0 + \beta(I_u + I_e + \varepsilon C) + \gamma_3 u_2)S] \\ + \lambda_2 [(\beta(I_u + I_e + \varepsilon C))S - Z_0 E] + \lambda_3 [\sigma E - Z_1 I_u] + \lambda_4 [\sigma E - Z_2 I_e] + \lambda_5 [-\mu\omega v(1-u_1)C + q(\gamma_0 I_u + \gamma_1 I_e) - Z_3 C] \\ + \lambda_6 [\alpha_1 I_u + \alpha_2 I_e + \alpha_3 C - Z_4 T] + \lambda_7 [\mu(1-\omega) + \gamma_3 u_2 S - Z_5 V] \quad (3.10)$$

$$\lambda_1' = -A_1 + \lambda_1 [\mu_0 + \beta(I_u + I_e + \varepsilon C) + \gamma_3 u_2] - \beta(I_u + I_e + \varepsilon C)\lambda_2 - \gamma_3 u_2 \lambda_7 \quad (3.11)$$

$$\lambda_2' = Z_0 \lambda_2 - (\lambda_3 + \lambda_4)\sigma \quad (3.12)$$

$$\lambda_3' = \beta S(\lambda_1 - \lambda_2) + Z_1 \lambda_3 - q\gamma_0 \lambda_5 - \alpha_1 \lambda_6 \quad (3.13)$$

$$\lambda_4' = \beta S(\lambda_1 - \lambda_2) + Z_2 \lambda_4 - q\gamma_1 \lambda_5 - \alpha_2 \lambda_6 \quad (3.14)$$

$$+ \mu \omega v (1 - u_1) (\lambda_3 - \lambda_1) + \mu \omega v \lambda_1 - \varepsilon \beta S (\lambda_1 - \lambda_2) + Z_3 \lambda_3 - \alpha_3 \lambda_6 \quad (3.15)$$

$$(3.16)$$

$$(3.17)$$

transversality conditions $\lambda_i(t_f) = 0$ ($i = 1, \dots, 7$, t_f is the end time). Using the Hamiltonian, we obtain the conditions.

$$\frac{\partial H}{\partial B_1} = 0 \quad (3.18)$$

$$\frac{\partial H}{\partial B_2} = 0 \quad (3.19)$$

Numerical Solution

For 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 [13].

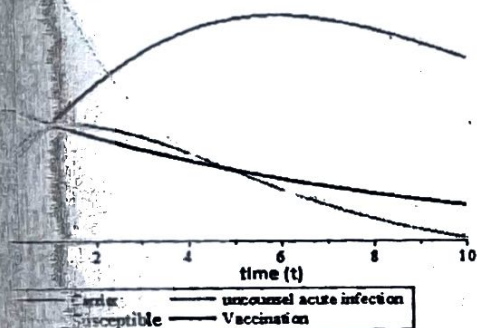


Figure 2: Graph of Carrier, Acute uncounsel, Susceptible and Vaccination at $u_1=0$, $u_2=0$

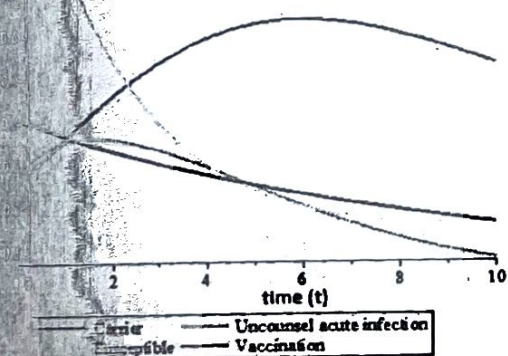


Figure 4: Graph of Carrier, Acute uncounsel, Susceptible and Vaccination at $u_1=0.1$, $u_2=0$

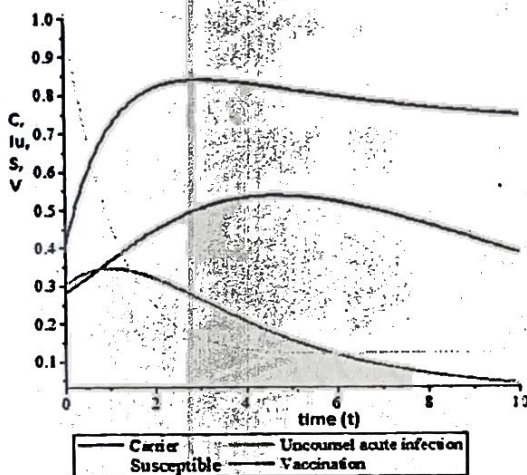


Figure 3: Graph of Carrier, Acute uncounsel, Susceptible and Vaccination at $u_1=1$, $u_2=0.9$

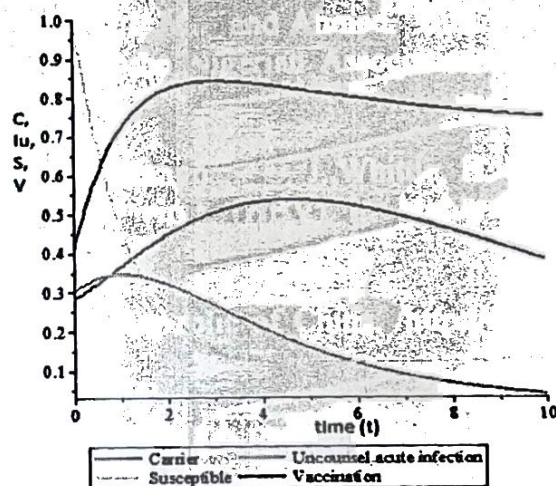


Figure 5: Graph of Carrier, Acute uncounsel, Susceptible and Vaccination at $u_1=0.1$, $u_2=0.9$

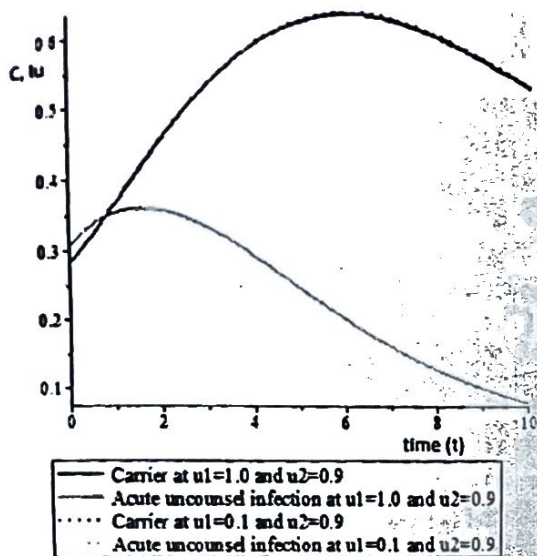


Figure 6: Graph showing the sensitivity in Carrier and Acute uncounsel infectious in figure 2 and 4

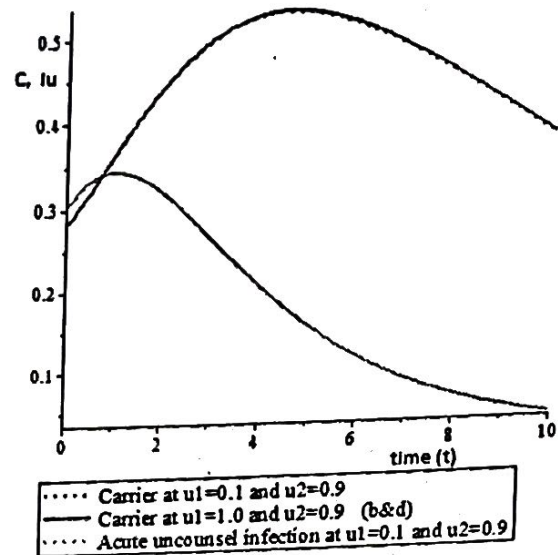


Figure 7: Graph showing the sensitivity in Carrier and Acute uncounsel infectious in figure 3 and 5

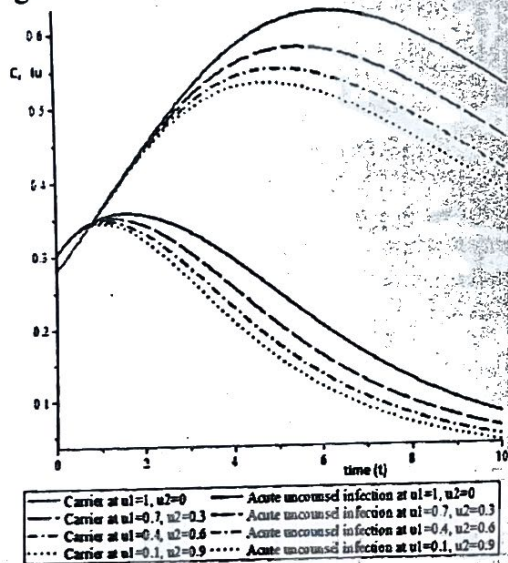


Figure 8: Graph showing the sensitivity in Carrier and Acute uncounsel infectious for different values of control

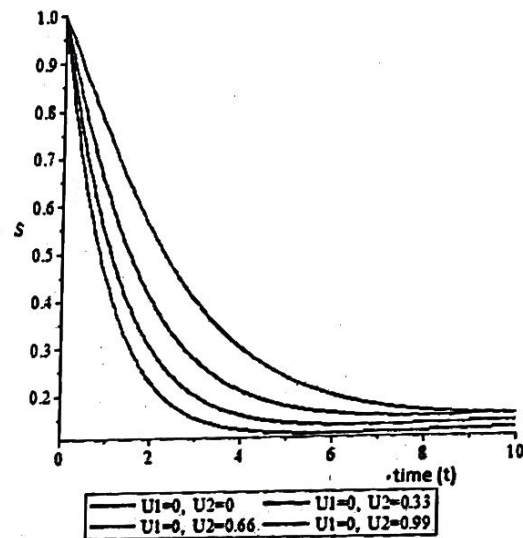


Figure 9: The plot shows the change in Susceptible populations at different values of control

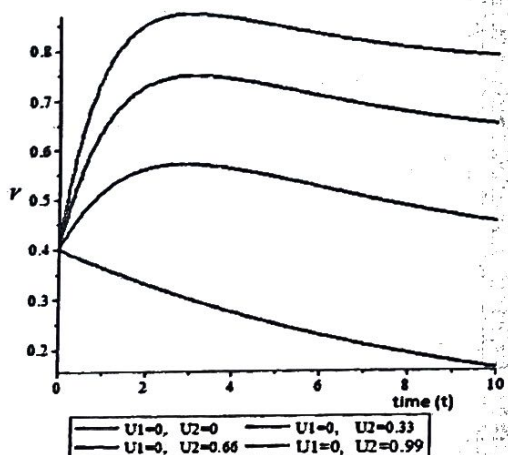


Figure 10: The plot shows the change in Vaccination populations at different values of control

Discussion of Results

and the relationship between the two control parameters (the rate of prevention or eradicates of mother to child u_1 and the cost of controlling the vaccination u_2) in the model, we solved the optimal control problem when $u_1 = 0$ (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 $u_2 = 0$ and also considering when $u_1 = 0.1$ and $u_2 = 0.9$ (Figure 5). The numerical solution profiles which we obtained are Figure (2, 3, 4, 5). The four scenarios show two major significant difference, Figure 2 and 4, Figure 3 and 5, show small differences as portrayed by Figure 6 and 7. We own this change to the control parameter u_1 , while the change (Figure 8) recorded is due to the cost effectiveness of the vaccination strategies u_2 . Moreover, we also show the control parameters on both the Susceptible and Vaccination population in Figure 9 and Figure 10 respectively.

Conclusion

In this paper, we proposed eight compartmental models of Hepatitis B virus infection with two controls; the prevention or of mother to child transmission (u_1) and cost of controlling the vaccination strategies employed (u_2). The positivity model is obtained. Thus, we formulate an optimal control problem and solved it using the Pontryagin's maximum. The results established shows that effort put in place in subduing or eliminating the birth of carrier by prenatally carrier mother is not a sufficient intervention to employ. However, three-dose vaccine administered to the newborn designed at regular interval is an effective way of curbing the outbreak. The study concluded that Prophylactic and vaccination is an efficient way to curb the epidemic.

References

- Ganem, D., & Prince, A. M. (2004). Mechanics of disease: hepatitis B virus infection-natural history and clinical consequences. *New England Journal of Medicine*, 350 (11), 1118-1129.
- Barker LF, Shulman NR, Murray R, Hirschman RJ, Ratner F, Diefenbach WC, Geller HM (1996). 'Transmission of serum hepatitis. 1970'. *Journal of the American Medical Association* 276(10):841-844.doi:10.1001/jama.276.10.841.
- Chang M H (2007) Hepatitis B virus infection. *Semin Fetal Neonatal Med* 12 (3): 606-67.doi:10.1016/j.siny.2007.01.013.
- Edmunds, W.J., Medley, G.F., Nokes, D.J., Hall, A.J., Whittle, H.C., (1993). The influence of age on the development of the hepatitis B carrier state. *Proc. R. Soc. Lond. B* 253, 197001.
- WHO World Health Organization Report,(2004)
- Dotia, A.K., Ibrahim, M.O., Bello, K.A., Yisa, B.M., and Ahmed, B.M. (2015). Global Stability of HBV Epidemic Model, *Transaction of the Nigerian Association of Mathematical Physics*, 1, 273-280.
- Edmund, W. J., Medley, G. F., Nokes, D. J., O'callaghan, C. J., Whittle, H. C., Hull, A. J. (1996). Epidemiological patterns of hepatitis B virus (HBV) in highly endemic areas. *Epidemiology and Infection*, 117 (2), 313-325.
- MOHC, (2009). Ministry of Health of the People Republic of China. /http://www.moh.gov.cn/publicfiles//business/htmlfiles/zwgkzt/pyq/list.htmS.
- MMWR, (2007). Progress in hepatitis B prevention through universal infant vaccination China. *Morbidity Mortality Weekly Rep.* 56 (18), 441-445.

- [10] Lan Zou, Weinian Zhang Shigui Ruan, (2010). Modeling the transmission dynamics and control of hepatitis B virus in China, *Journal of Theoretical Biology* 262 (2010) 330-338 control measures. *J. Viral. Hepat.* 11, 97-107.
- [11] Hahne, S., Ramsay, M., Balogun, K., Edmunds, W.J., Mortimer, P., (2004) Incidence and routes of transmission of hepatitis B virus in England and Wales, 1995-2000: implications for immunization policy. *J. Clin. Virol.*, 29 (4), 211-220.
- [12] Sirajo A., Ninuola I. A., Omotayo B. A., and Usman Y.A. (2013) Mathematical Analysis of the Control of Hepatitis B Virus in a Population with Vital Dynamics. *The Pacific Journal of Science and Technology*, 14 (1), 188-204.
- [13] Maple 18 Software. (2014) Waterloo Maple Inc. Ontario, Canada