WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Basic Properties of Mathematical Model of Hepatitis B Dynamics with Vaccination, Treatment and Post Exposure Prophylaxis

[1]Ogbuagu E. M., [2]Jackreece P. C. and [3]Nzerem F. E.

Department of Mathematics and Statistics, University of Port Harcourt.
Email: [1]elomaryethel@gmail.com, [2]prebo.jackreece@uniport.edu.ng
DOI: https://doi.org/10.55248/gengpi.4.623.46990

ABSTRACT

In this work, we studied mathematical modeling of hepatitis B dynamics with vaccination, antiviral treatment and post exposure treatment. We formulated the model and studied its properties to show the biological feasibility. We found the basic reproduction number and discussed the sensitivity analysis. The model was demonstrated with the aid of a flow diagram. The disease free equilibrium was determined and the basic reproduction number was computed. Numerically the sensitivity of the intervention parameters to the basic reproduction number was studied using python. The result showed that the basic reproduction number R_0 *is a* decreasing function of the post exposure treatment rate, that is increase in the rate of post exposure treatment reduces the R_0. However, The study concludes that high rate of post exposure prophylaxis treatment or combining it with vaccination and treatment at chronic stage vaccination are crucial to the success of HBV disease control and eradication.

Keywords: Hepatitis B virus (HBV); Basic reproductive number, Boundedness of solution, Sensitivity analysis.

1. Introduction

Hepatitis is referred to as liver inflammation caused by viruses, alcohol or substances, exposure to toxins, and certain diseases and bacterial infection (Ganem et al, 2004). In the late 90s, Hepatitis can also result from the disorder of autoimmune, where the body mistakenly sends diseases – fighting cells to attack its own healthy tissues (Baker et al, 1996).

Hepatitis reduces the liver's ability to perform life preserving functions, including filtering harmful infection agents from the blood, storing blood sugar and converting it to usable energy forms, and producing many proteins necessary for life (Edmunds et al, 1993).

According to WHO (2021), there are five main strains of the hepatitis virus, referred to as types A, B, C, D and E. They all causes liver diseases and they also differ in modes of transmission, severity of the illness, geographical distribution and prevention methods. Hepatitis B is a viral infection that attacks the liver, caused by hepatitis B virus (HBV). It can cause both acute and chronic diseases and can put people at high risk in death from cirrhosis and liver cancer.

The HBV infection is of two kinds, the acute hepatitis and the chronic hepatitis. The acute infection stays up to six months and the infected individual recovers or becomes a chronic carrier of the HBV. Most times, the chronic infected patient of HBV is infected either vertically or horizontally. According to WHO (2021), some infected adults will recover naturally within the first year of infection without showing any symptoms of the diseases. This is the dangerous aspect of Hepatitis B infection since individuals could be infected but not aware of it thereby placing them at a higher risk of transmitting the virus (Rodriguez, 2016).

Vertical transmission is the most common mode of transmission of hepatitis B virus (HBV). Infants get infected through if the mother is HBsAg and HBeAg positive but the percentage of transmission rate reduces if the mother is HBsAg positive but HBeAg negative or anti HBe positive. Even if perinatal infection does not occur, the infant has a high risk of developing infection from other family contacts; hence prophylaxis of all infants born to HEsAg positive mothers is, therefore recommended regardless of mothers' HBe or anti HBe status.

Mathematical modelling is an important tool that is useful in the control of human and animal infectious diseases. It is of great interest to understand the connections between the HBV, the human immune responses of the body, effectiveness of the vaccine, waning of vaccine, and response to treatment especially the post exposure treatment of the HBV. Mathematical models can be used to gain a clear understanding of disease transmission dynamics and the intervention measures.

Several authors have studied HBV transmission dynamics with focus on the influence of prevention and control measures.

In Alrabaiah et al. 2020, they proposed SEACTVR model which stand for Susceptible, Exposed, Acute infected, Chronic infected, treatment class, vaccinated class and recovered class respectively. They assumed that there are some individuals who received treatment and still go to chronic class due to failure in treatment, that some treated individual recovers and become permanently immune. (include method of analysis and result)

Kamyad et al. (2014) formulated a $SEICR$ model where they firstly study two controlling variables are considered (vaccination and treatment) in order to prevent the spread of the HBV and finally to put down the infection from the population.

Zhang et al (2015) formulated a $SEACR$ model in modelling and analyzing the Transmission dynamics of HBV epidemic in Xinjiang, China. Incorporating the recruitment into susceptible population is simplified as new birth. Just like Alrabaiah et al ( ), they assumed infected people who experience failure in treatment move back to chronic state.

Otoo et al. (2021) developed a six compartments model S$EITVR$ to study and analyze the dynamics of hepatitis B with optimal control. They considered recover as not being totally immune, assumed that the vaccine wane after a long period of time and developed a latent class.

In their study on mathematical modelling of transmission dynamic and optimal control of isolation, vaccination and treatment for hepatitis B virus, Olajide et al (2018) created an $SEICRV$ (Susceptible- Exposed- Infective- Carrier- Recovered) model of HBV. They incorporate waning of vaccine – induced immunity, disease transmission with constant recruitment.

Zou et al (2010) proposed a SLICVR model where they took into account that vaccination does not imply permanent immunity and that new born to carrier mothers infected at birth proceed to carrier state immediately. Kimbir et al (2014) formulated SLICVR mathematical model for the transmission dynamics of hepatitis B virus (HBV) infection incorporating vaccination and treatment as control parameter by extending the model of Zou et al. Here they assumed and quoted that chromic carriers are treated, that acute infections are not subjected to antiviral treatment because of possibility of relapse and resistance (WHO, 2001), the newborns to carrier mothers infected at birth first enter the latent class and that the treated individuals recovers. In this paper, we aim to investigate the transmission dynamics of HBV in the presence Post exposure treatment, vaccination and antiviral treatment.

2 Model Formulation

We consider the interventions measures i.e., vaccination, treatment and post exposure prophylaxis (PEP) of Hepatitis B in the model. Let the total population be $N(t)$, Exposed $E(t)$, Acute infected $A(t)$, chronic carrier inflections $C(t)$, Recovered $R(t)$ and vaccinated $V(t)$, keeping the characteristics of HBV; we also impose the following general assumptions;

2.1 Basic Assumptions

a. Recovered individuals from acute and chronic compartments have permanent immunity.

b. All the new born from non-carrier mothers gets vaccinated/immunized and goes to the vaccinated compartments.

c. All the new born from carrier mothers gets Post Exposure Prophylaxis of Hepatitis B goes to the vaccinated compartments.

d. Individual who are aware of being exposed to HBV, takes the Post Exposure Prophylaxis of Hepatitis B and move to vaccinated class.

e. The only means of influx to the population in by birth and only way to exit the population is by natural death or death induced by HBV.

f. The vaccine efficacy is 100% but wanes after a long period of time

g. There are no immigrants and emigrants.

The total population in of the model S, E, A, C, V, R a time t is $N(t)$ is

$$N(t) = S(t) + E(t) + A(t) + C(t) + V(t) + R(t) \qquad (1)$$

Individuals are recruited into the population at constant rate B. The susceptible population increases by the recruitment of individuals who are not vaccinated at rate $B\omega_0$, where ω_0 is the population of non- vaccinated recruitment, while the complementary proportion $(1-\omega_0)B$ is protected, that is vaccinated and enters the class of vaccinated individuals V. The population of vaccinated individuals increased by the vaccination of the new born babies at the rate

$(1-\omega_0)B$, and vaccination of susceptible individuals at constant rate γ_3. Since the vaccination does not confer permanent immunity to all vaccine recipient, vaccinated individuals lose their immunity when the vaccine wanes and return to the susceptible class S at a constant rate φ.

The susceptible decrease due to HBV infection at rates λS, where λ in the force of infection given by

$$\lambda = \frac{\beta(A+\varepsilon C)}{N} \qquad (2)$$

Where B is the transmission coefficient of HBV and $0 < \varepsilon < 1$ is a modification parameter that takes into account the fact that acute are most infectious than chronic HBV. After infection, newly infected individuals move to the exposed class. Exposed individuals who are aware of being exposed takes post-exposure vaccine and move to vaccinated class the rate γ_2, while those who are not aware become infectious and move from exposure class to Acutely infected class at a constant rate σ. γ_1 is the rate at which individuals leaves the acutely infected class, q is the proportion that leave acute and

progress to chronic class and $1-q$ is the proportion that leave acutely infected class and progress to recovered when treated. At the rate α, individuals leaves chronic class to recovered when treated or moves to recovered class at the rate θ when HBV is naturally cleared without treatment. Egress out of the population is by natural and HBV related mortality only at the rate μ_0 and μ_1 respectively.

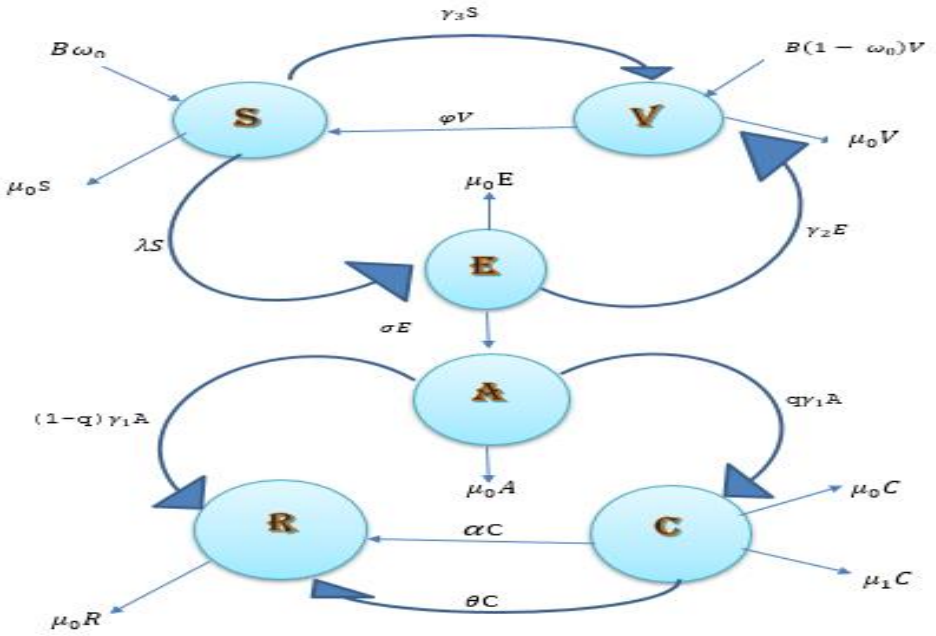

Figure 1: Structure of the model.

2.2 The Model Equation

From the flow chart in figure 1, the HBV transmission model is described by the following system of non-linear ordinary differential equation.

$$S' = Bw_0 + \varphi V - (\lambda + \gamma_3 + \mu_0)S$$

$$E' = \lambda S - (\gamma_2 + \mu_0 + \sigma)E$$

$$A' = \sigma E - (\mu_0 + \gamma_1)A \qquad (3)$$

$$C' = q\gamma_1 A - (\mu_0 + \mu_1 + \alpha + \theta)C$$

$$V' = B(1-w_0) + \gamma_3 S + \gamma_2 E - (\mu_0 + \varphi)V$$

$$R' = (1-q)\gamma_1 A + (\alpha + \theta)C - \mu_0 R$$

Variables	Interpretation	Units
$S(t)$	Number of susceptible individuals at time t	individuals
$E(t)$	Number of Exposed individuals at time t	individuals
$A(t)$	Number of acutely infected individuals at time t	individuals
$C(t)$	Number of chronic carrier individuals at time t	individuals
$V(t)$	Number of vaccinated individuals at time t	individuals
$R(t)$	Number of recovered individuals at time t	individuals

2.3.1 Positivity of the Solutions

For model to be epidemiological meaningful, it is important to prove that its entire state variables are positive for all time. In other words, solutions of the model with positive initial data remain positive for all time $t > 0$.

Theorem 1

Let the initial data be

$$\{S(0) > 0, E(0) > 0, A(0) > 0, C(0) > 0, V(0) > 0, R(0) > 0\}$$

Then the solution set $\{SEACVR\}(t)$ of the model system is non negative $\forall\, t \geq o$

Proof

Let's Define

$$t_1 = sup\{t > 0 : S(0) > 0, E(0) > 0, A(0) > 0, C(0) > 0, V(0) > 0, R(0) > 0\}$$

The initial conditions above added to continuity of all the function S, E, A, C, V, R ensures the existence of t_1. If $t_1 = \infty$, then all solutions of the system are positive. Suppose $t_1 < \infty$ $(i.e\ t_1$ is finite), then there is a least one solution of

$$S(t), E(t)A(t), C(t), V(t), R(t)$$

which will be equal to zero at value t_1. (From the definition of t_1 as a supremum). Considering the first equation of the system (3)

$$S'(t) = Bw_0 + \varphi V - (\lambda + \gamma_3 + \mu_0)S(t)$$

Then we know that $v\, t \in (0, t_1), Bw_0 + \varphi V \geq 0$, Then one can deduce that

$$S'(t) = (\lambda(t) + \gamma_3 + \mu_0)S(t) \geq 0 \qquad (4)$$

From the above equation the integrating factor is

$$exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)$$

Then, multiplying the both sides of the equation by the integrating factor yields

$$S'(t).\ exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right) + (\lambda + \gamma_3 + \mu_0)S(t).exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)$$

$$= exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)\left(S'(t)(\lambda(t) + \gamma_3 + \mu_0)S(t)\right)$$

$$= \frac{d}{dt}[S(t)\ exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)]$$

Now, from the equation (3.3.1), one has that

$$\frac{d}{dt}\left[S(t)\ exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)\right] \geq 0$$

Integrating the above from $0\ to\ t_1$ that is

$$\left[S(t)\ exp\left(\int_0^t \lambda(s)ds + (\mu_0 + \gamma_3)t\right)\right]_0^{t_1} \geq 0$$

Then, one can deduce that

$$\left[S(t_1)\ exp\left(\int_0^{t_1} \lambda(s)ds + (\mu_0 + \gamma_3)t_1\right) - S(0)\right] \geq 0$$

$$\Longrightarrow \quad S(t_1)\ exp\left(\int_0^{t_1} \lambda(s)ds + (\mu_0 + \gamma_3)t_1\right) \geq S(0)$$

$\Longrightarrow$ $S(t_1) > 0$ since $S(0) > 0$ and thus contradicts the fact that $S(t_1) = 0$

Hence $S(t_1) > 0, \forall\, t \geq 0$

Let now consider the second equation of the model system equation (3):

$$E' = \lambda S - (\gamma_2 + \mu_0 + \sigma)E$$

With the same assumption that $E(t_1) = 0$. From the equation, since $\lambda S \geq 0\ \forall\, t \in (0, t_1)$, One has that

$$E' + (\gamma_2 + \mu_0 + \sigma)E \geq 0 \qquad (5)$$

From which the integrating factor is

$$e^{\int(\gamma_2 + \mu_0 + \sigma)dt}$$

Multiplying both sides with the integrating factor, we have

$$E'.e^{\int(\gamma_2+\mu_0+\sigma)dt} + (\gamma_2 + \mu_0 + \sigma)E.e^{\int(\gamma_2+\mu_0+\sigma)dt} \geq 0$$

$$= \frac{d}{dt}\left[E(t)e^{(\gamma_2+\mu_0+\sigma)t}\right]$$

Then integrating the above equation from 0 to t_1, we have

$$E(t_1)e^{(\gamma_2+\mu_0+\sigma)t_1} - E(0) \geq 0$$

$\Longrightarrow$ $E(t_1) > 0$ and this contradicts that $E(t_1) = 0$. Hence $E(t_1) > 0 \; \forall \; t \geq 0$. Similarly, it could be deduced that $A(t) > 0$, $C(t) > 0$, $V(t) > 0$ and $R(t) > 0$, hence it is shown that the solutions of the equations in the system are all non-negative.

2.3.2 Boundedness of the Trajectories.

Since we are dealing with human population, and having proved that the solution of the system are positive $\forall \; t > 0$. Then we will analyze the model in a feasible region, that is a region in which the solution of the system of the equation is biological meaningful. By adding the equations of model system (3), one obtains the conservation law:

$$\frac{dN(t)}{dt} = B - \mu_0 N(t) - \mu_0 N(t) - \mu_1 C$$

and

$$\frac{dN(t)}{dt} = B - \mu_0 N(t) - \mu_0 N(t) - \mu_1 C \leq B - \mu_0 N(t)$$

(in the absence of the disease ($\mu_1 = 0$))

$$\Longrightarrow \quad \frac{dN(t)}{dt} \leq B - \mu_0 N(t)$$

$$\Longrightarrow \quad \frac{dN(t)}{B - \mu_0 N} \leq dt$$

Integrating the both sides, we have

$$\int -\frac{1}{\mu_0} ln(B - \mu_0 N) \leq t + A_1$$

$$\Longrightarrow \quad ln(B - \mu_0 N) \leq -\mu_0 t + A_1$$

$$\Longrightarrow \; B - \mu_0 N \geq A_2 \, e^{\mu_0 t}$$

$$\Longrightarrow \; B - A_2 \, e^{\mu_0 t} \geq \mu_0 N$$

$$\Longrightarrow \frac{B}{\mu_0} \geq N$$

Therefore, all the solutions of the system within the region

$$\Omega = \left\{(SEACVR) \in \mathbb{R}_+^6, N \leq \frac{B}{\mu_0}\right\} \qquad (6)$$

Now, we show that the region Ω is positively invariant with respect to the dynamical system (3). Recall that the dynamics of the total population satisfies.

$$\frac{dN(t)}{dt} \leq B - \mu_0 N(t),$$

That is

$$\frac{dN(t)}{dt} + \mu_0 N(t) \leq B.$$

From the equation above, the integrating factor becomes $e^{\mu_0 t}$. Then we have

$$\frac{dN(t)}{dt} \; e^{\mu_0 t} + \mu_0 N(t) \, e^{\mu_0 t} \leq B \, e^{\mu_0 t}$$

$$= \frac{d}{dt}[N(t)e^{\mu_0 t} \;] \leq B \, e^{\mu_0 t}$$

Integrating the both sides from 0 to t, we have

$$\int_0^t \frac{d}{dt}[N(t)e^{\mu_0 t} \;]dt \leq \int_0^t B \, e^{\mu_0 t} dt$$

$$= N(t)e^{\mu_0 t} - N(0) \leq \frac{B}{\mu_0}[\, e^{\mu_0 t} - 1]$$

$$\Longrightarrow \quad N(t) - N(0)e^{-\mu_0 t} \leq \frac{B}{\mu_0}[\, e^{\mu_0 t} - 1]\, e^{-\mu_0 t}$$

$$\Longrightarrow \quad N(t) \leq \frac{B}{\mu_0}[\, e^{\mu_0 t} - 1]\, e^{-\mu_0 t} + N(0)e^{-\mu_0 t}$$

$$\Longrightarrow \quad N(t) \leq \frac{B}{\mu_0} - \frac{B}{\mu_0}e^{-\mu_0 t} + N(0)e^{-\mu_0 t}$$

$$\Longrightarrow \quad N(t) \leq \frac{B}{\mu_0} + (-\frac{B}{\mu_0} + N(0))e^{-\mu_0 t}$$

$$\Longrightarrow \quad N(t) \leq \frac{B}{\mu_0} + \left(N(0) - \frac{B}{\mu_0}\right)e^{-\mu_0 t}$$

$$\lim_{t\to\infty} N(t) \leq \frac{B}{\mu_0} + \left(N(0) - \frac{B}{\mu_0}\right)e^{-\mu_0 t}$$

$$= N(t) \leq \frac{B}{\mu_0} \;\; \forall\, t \geq 0$$

Hence the trajectories of the model system (3) are bounded in the region Ω, this means that the system of equations of (3) remains in Ω for all $t > 0$ and thus the model is biologically meaningful, epidemiologically and mathematically well posed in the interior of the domain Ω.

3.1 Sensitive Analysis and Basic Reproduction Number,R_0

To establish analytic threshold for when vaccination and treatment are society's prudent choice, we consider the case of a population at the time of eradicating HBV. Mathematically, we must consider the disease free equilibrium (DFE). The disease-free equilibrium (DFE) for an epidemiological model is equilibrium such that the disease is absent in the community. Thus, if $D_0 = (S_0,\ E_0,\ A_0, V_0, R_0)$ is the DFE of model system (3), then $E_0 = A_0 = 0$.

As a consequence of model system (3), $R_0 = 0$ with S_0 and V_0 being solutions of the system:

$$B\omega_0 + \varphi V_0 - (\mu_0 + \gamma_3)S_0,$$

$$B(1 - \omega_0) + \gamma_3 S_0 - (\mu_0 + \varphi)V_0,$$

This has the unique solution:

$S_0 = \frac{B(\varphi+\omega_0\mu_0)}{\mu_0(\mu_0+\varphi+\gamma_3)}$ and $V_0 = \frac{B(\mu_0(1-\omega_0)\gamma_3)}{\mu_0(\mu_0+\varphi+\gamma_3)}$

and

$$N_0 = S_0 + V_0 = \frac{B}{\mu_0}.$$

Then using the next generation matrix, the basic reproductive number is

$$\mathrm{R}_0 = \frac{\sigma S_0\beta((\mu_0+\mu_1+\alpha+\theta)+\varepsilon q\gamma_1)}{(\gamma_2+\mu_0+\sigma)(\mu_0+\gamma_1)(\mu_0+\mu_1+\alpha+\theta)N_0}. \qquad (7)$$

4. Numerical Simulation

Table 1 Variables of the system (3) and its interpretation

Parameters	Interpretation	Estimate
B	Recruitment	0.9121
μ_0	Natural mortality	0.0121
μ_1	HBV-related mortality	0.0091
ω_0	Proportion of non-vaccinated recruitment	0.26
σ	Rate of moving from exposed to acute state	0.005
γ_2	Post exposed vaccinated of the exposed individuals	0.55
φ	Vaccination rate of the susceptible individuals	0.6
β	Transmission coefficient	0.45
ε	Reduced transmission rate relative to acute infection by carriers	0.5
γ_1	Rate of moving from acute to other compartments	0.44
q	Rate of moving from acute to carrier	0.5

α	Rate of moving from carrier to immune by treatment	0.6
θ	Rate of moving from carrier to immune naturally	0.6
γ_3	Rate of susceptible get vaccinated	0.74

Table 2 Parameters of the model system (3) and its interpretation

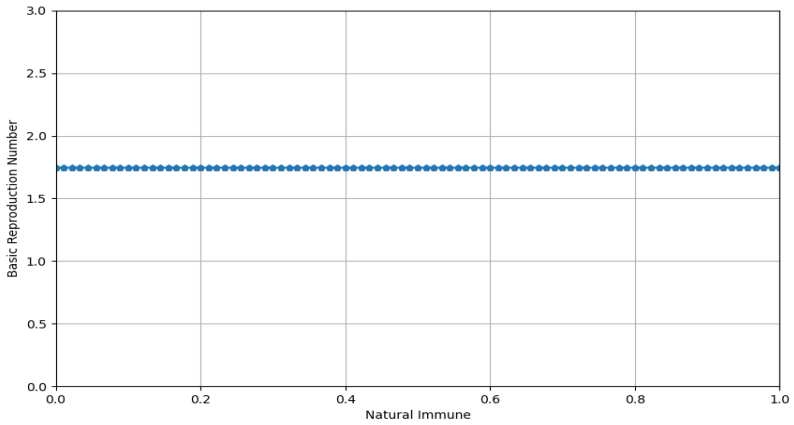

Figure 2: Impact of natural immune of the chronic infected individuals on the basic reproduction. Other parameters values are as in the Table 1.

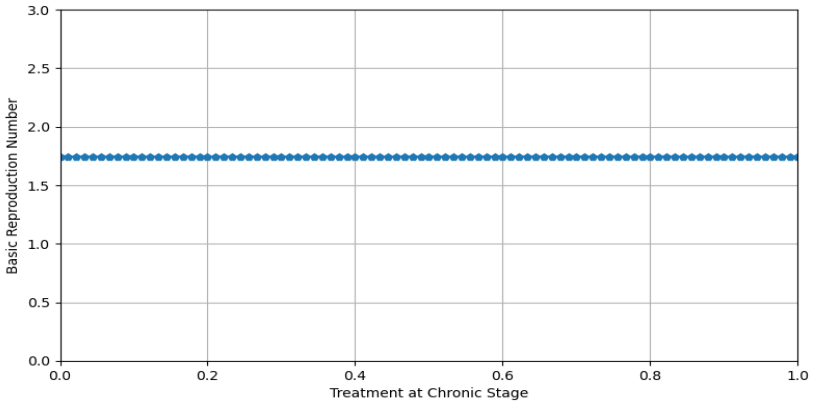

Figure 3: Impact of Treatment of the chronic infected individuals on the basic reproduction. Other parameters values are as in the Table 1.

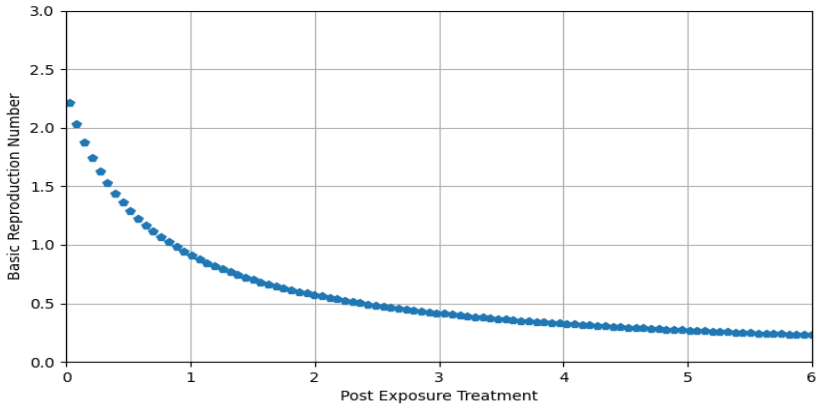

Figure 4: Impact of post exposure treatment on the basic reproduction. Other parameters values are as in the Table 1.

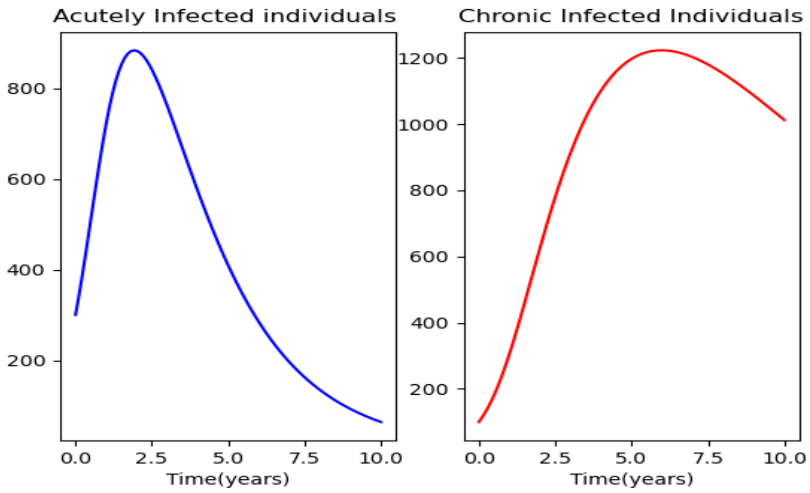

Figure 5: Numerical simulation of acutely infected individuals and Chronic infected individuals in the absence of immune, Treatment, vaccination and post exposure treatment

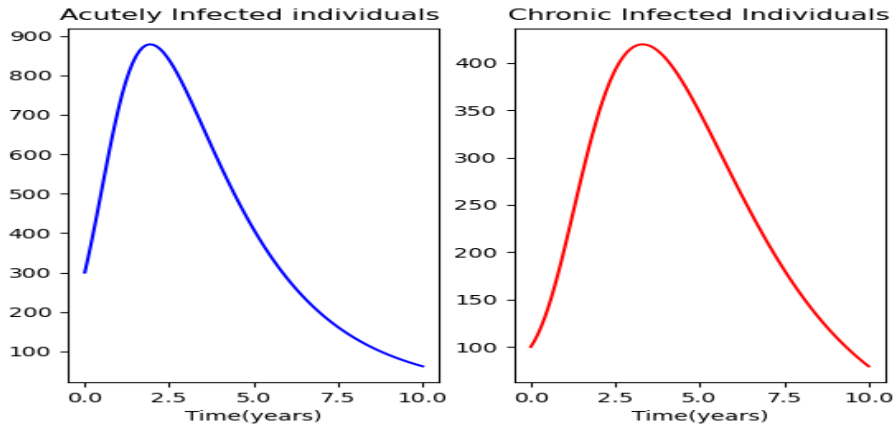

Figure 6: Numerical simulation of Acutely individuals and Chronic individuals in the presence of immune and absence of Treatment, vaccination and post exposure treatment, high force of infection, natural immune, $\theta = 0.55$ and the rest of the values from the table 2

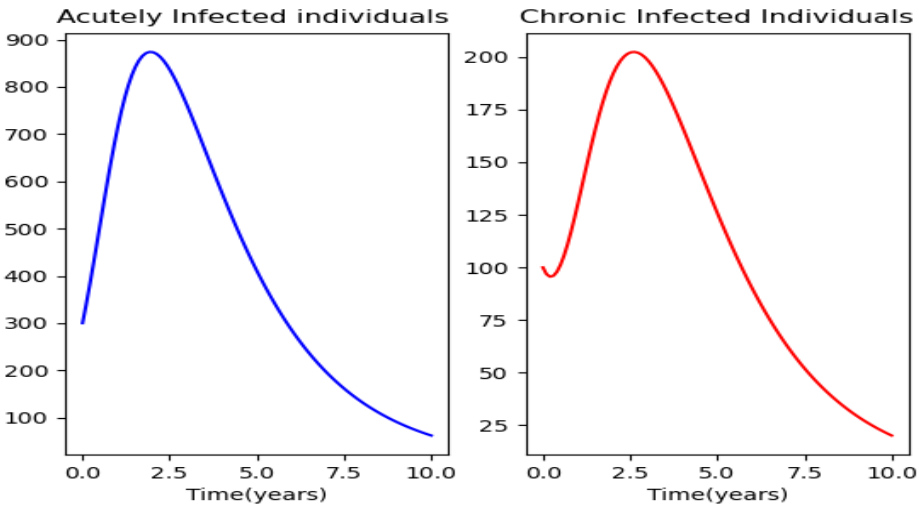

Figure 7: Numerical simulation of Acutely infected individuals and Chronic infected individuals in the presence of immune and treatment and absence of vaccination and post exposure treatment with high force of infection, natural immune, $\theta = 0.55$, Treatment, $\alpha = 0.83$ and the rest of the values from the table 2

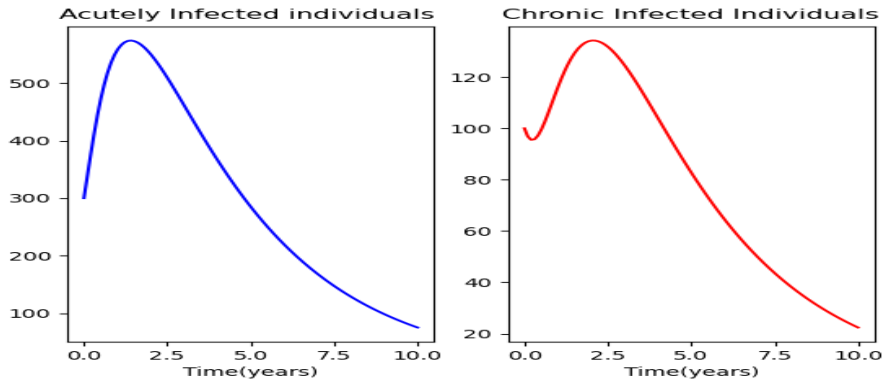

Figure 8: Numerical Simulation of Acutely infected individuals and Chronic infected individuals in the presence of immune, treatment and vaccination, and absence of and post exposure treatment with high force of infection, natural immune, $\theta = 0.55$, Treatment, $\alpha = 0.63$, vaccination,$\gamma_3 = 0.64$, $\omega_0 = 0.66$ and the rest of the values from the table

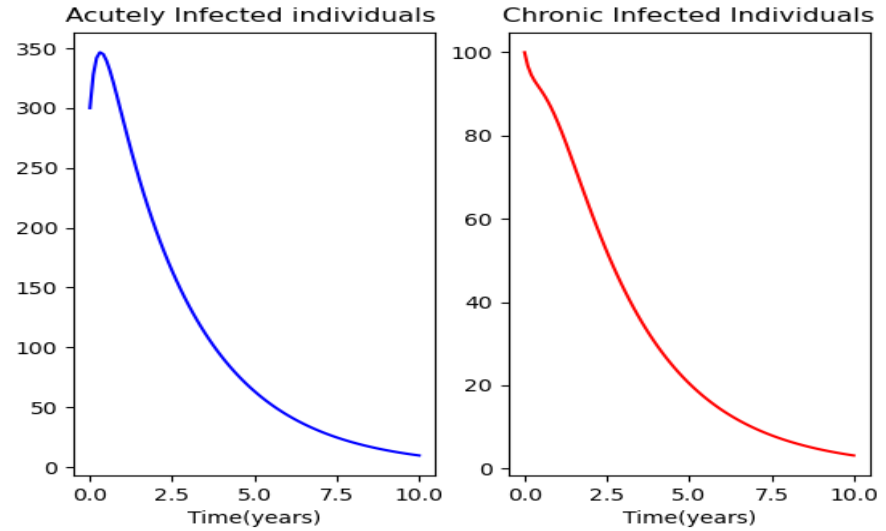

Figure 9: Numerical simulation of acutely infected individuals and Chronic infected individuals in the presence of immune, treatment, vaccination and post exposure treatment. natural immune, $\theta = 0.55$, Treatment, $\alpha = 0.83$, vaccination, $\gamma_3 = 0.74$, $\omega_0 = 0.26$, post exposure treatment, $\gamma_2 = 0.75$ and the rest of the values from the table 1

5. Discussion and Conclusion

In this study, we studied a mathematical model of hepatitis B dynamics which incorporates vaccination, treatment at acute and chronic stage and post exposure treatment. The results of the numerical simulation of the study are discussed as follows;

The interventions parameters have an important effect the basic reproduction number, R_0 . Numerically we explored the sensitivity of the immune, treatment on the chronic stage and the post exposure treatment parameters that is α, θ *and* γ_2 respectively.

figure 2 and figure 3 shows that the basic reproduction number which is greater one and remain constant at a particular spot as the parameter for the rate of getting immune and treatment at chronic stage increases.

It is observed from figure 4 that as the rate of post exposure treatment increases, the basic reproduction number decreases

Considering a state where there is no immune to hepatitis B virus, no treatment, no vaccination and no post exposure treatment. It was observed that the number of acutely infected individuals in figure 5 increased first and later started decreasing after a period of time. The number of chronic infected individuals reacted the same way but the increment was so much and decreases after a period of time. In the presence of immune and absence of treatment, vaccination and post exposure treatment. it was observed from figure 6 that the number acutely infected individuals reacted same way as in the case of the absence of immune, Treatment, vaccination and post exposure treatment. While the chronic infected individual increased and took time to decrease but not as much time as in the case of the absence of immune, Treatment, vaccination and post exposure treatment.

Figure 7 showed that due to the presence of immune and treatment and absence of vaccination and post exposure treatment, the number of acutely infected reacted the same as in the case of presence of immune and absence of Treatment, vaccination and post exposure treatment. But the number of the chronic infected individuals had hundred percent increment unlike in the case of presence of immune and absence of Treatment, vaccination and post exposure treatment and the case of the absence of immune, Treatment, vaccination and post exposure treatment up to four hundred percent and six hundred percent respectively.

For the case where there is presence of immune, treatment and vaccination, and absence of post exposure treatment, figure 8 showed that the number of acutely infected individual increased and decreases after some period of time. The number of chronic infected individuals had a very slit decrease, increased after period of time and decreases again after a period of time.

Lastly, considering the case where there is presence of immune, treatment, vaccination and post exposure treatment. The figure 9 showed that number of chronic infected individuals also decreases without having increment but not instantly. The number acutely infected individuals had a slit increment before decreasing and the number of vaccinated individuals increased instantly and that of recovered individuals increases with time.

Reference

Akbari, R., Kamyad, A. V, Heydai, A. A., and Heydan, A.(2016) Analysis of a diseases free equilibrium of hepatitis B model. *Sahend communication in mathematical analysis* vol. no. 2, (2016) 1 -11.

Alrabaiah, H., Safi, M. A., DarAssi, H. M., Al-Hdaibat, B., Ullah, S., Khan, M., and Shah, S. A (2020). Optimal control analysis of hepatitis B virus with treatment and vaccination.

Results in Physics, 2020, 2211-3797, https://doi.org/10.1016/j.rinp.2020.103599

Anwarud D., Li Y J, and Liu Q, Viral dynamics and control of hepatitis B virus (HBV) using an epidemic model, *Alexandria Engineering Journal*, 2020, **59**(2): 667–679.

Abubaka, A. Borkor, R. N., Musah, A. and Owusu, F. K.(2021) Mathematical Modeling of Transmission Dynamics with Periodic Contact Rate and Control by Different vaccination

Rates of Hepatitis B Infection in Ghana. *Asian Research Journal of Mathematics 17(8)* 54-75, 2021; Article no.ARJOM.74967 *ISSN: 2456-477X*

Ashish, G. (2016) Mathematical Modelling of Hepatitis D virus, *University of New South Wales* 2016) (Dissertation)

Ater, M., Mast, E.(1994). The epidemiology of viral hepatitis in United States: Gastroenterl clin. *North America*. 1994, 23:437 - 440

Bertoletti A, Maini M. K, Ferrari C. The host-pathogen interaction during HBV infection: immunological controversies. *Antivir Ther*. 2010;15 Suppl 3:15-24. doi: 10.3851/IMP1620. PMID: 21041900.

Chataa, P. , Fara, N., and Samuel, N. M. (2021) Mathematical modelling of the dynamics of HBV in presence of imperfect vaccination. *J. Math. Comps. Sci.II* (2021), No. 6, 6949 – 6979 Center of Disease Controol and Prevention Hepatitis B faqs for the public(2021).

Chinebu, T. I., Ezennorom, E. O., and Godwin C. E. Mbah.(2018). A Mathematical Model of the Dynamics of Hepatitis B Virus (HBV) Infection with Controls. International Journal of Trend in Scientific Research and Development . 2018, Vol. 2, Issu. 5, page 1654 – 1677

Chisari F. V. 2000. Rous-Whipple award lecture. Viruses, immunity, and cancer: lessons from hepatitis B. *Am. J. Pathol.* 156:1117–1132.

Chuang W. L, Chang W. Y, Lu S. N, Su W. P, Lin Z. Y, Chen S. C, Hsieh M. Y, Wang L. Y, You S. L, Chen C. J. The role of hepatitis B and C viruses in hepatocellular carcinoma in a hepatitis B endemic area. A case-control study. Cancer. 1992 Apr 15;69(8):2052-4. doi:10.1002/1097-0142(19920415)69:8<2052::aid-cncr2820690808>3.0.co;2-n. PMID: 1311978.

Dontwi, K., Obeng-Denteh, W., Obiri-Apraku, L. and Andam, E. A. (2014). Modelling hepatitis B in a high prevalence district in Ghana. British Journal of Mathematics & Computer Science, 4(7), 969-988.

Diekmann, J.A.J, Heesterbeek, J.A.P. (1990). The definition and the computation of the basic reproduction ratio in models for infectious diseases in heterogeneous populations. *J. Math. Biol.*, 28:365, 1990.

Hussan, A., Mohammad, A. S., Mohammad, H. D., Hashor, A. H., Saifi, U., Mohammad, A. K. And Syed, A. A. (2020). Optimal control f Hepatitis B virus with treatment and vaccination. Result in Physics, vol. 19(2020) 103599

Hou, J., Liu, Z. and Gu, F. (2005) Epidemiology and Prevention of Hepatitis B Virus Infection. International Journal of Medical Sciences, 2, 50-57.http://dx.doi.org/10.7150/ijms.2.50

Kimbir, A. R., Aboiyar, T., Abu, O. and Onah, E. S.(2015). Simulation of A Mathematical Model Of Hepatitis B Virus Transmission Dynamics In The Presence Of Vaccination and Treatment. Mathematical Theory and Modeling. ISSN 2224-5804 (Paper) ISSN 2225-0522 (Online) Vol.4, No.12, 2014

Kamyad, A. V, Akbari, R., Heydari, A. A, Heydari, A. Mathematical modelling of transmission dynamics and optimal control of vaccination and treatment for hepatitis B virus. Comput Math Methods Med. 2014;2014:475451. doi: 10.1155/2014/475451. Epub 2014 Apr 9. PMID: 24812572; PMCID: PMC4000643.

Lok AS, McMahon BJ; AASLD (American Association for the Study of Liver Diseases). AASLD Practice Guidelines. Hepatita cronică B: actualizarea recomandărilor terapeutice [AASLD Practice Guidelines. Chronic hepatitis B: update of therapeutic guidelines]. Rom J Gastroenterol. 2004 Jun;13(2):150-4. Romanian. PMID: 15229781.

Moneim, I. A. And Khalil, H. A.(2015) Modelling and Simulation of the Spread of HBV Disease with Infectious Latent . Applied Mathematics, 2015, 6, 745-753 MMWR, January 12, 2018, Vol 67,(1);1–31, Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. https://www.cdc.gov/mmwr/volumes/67/rr/rr6701a1.html

Olajide , A. J.. Afeez , A.. Oluwaseun , J. O. & , A. F. O. (2019). Mathematical of Transmission Dynamics and Optimal Control of Isolation, Vaccination and Treatment for Hepatitis B Virus . General Letters in Mathematics, 5 (3), 132-147, 10.31559/glm2018.5.3.3

Otoo, D., Isaac , A., Shaibu, O. And Elvis, K. D.(2021). Mathematical modelling and Analysis of the dynamics of hepatitis B with optimal control.

Communications in Mathematical Biology and Neurosience. 2021, 2021: 43, Issn: 2052 – 2541

Khan, T., Zaman, G., & Chohan, M. (2018) The transmission dynamic of different hepatitis B-infected individuals with the effect of hospitalization, Journal of Biological Dynamics, 12:1, 11-631, DOI: 10.1080/17513758.2018.1500649

Thornley, S., Bullen, C., and Roberts, M. (2008). Hepatitis B in a high prevalence New Zealand population: A mathematical model applied to infection control policy. J. Theor. Biol. 254, 599–603.*Biosciences*, 29{48:582{592, 2002.

World Health Organisation. Hepatitis B fact sheet. (2019). https://www.who.int/newsroom/factsheets/detail/hepatitis-b. Accessed 21 Mar 2021.

Yazie T. D, Tebeje M. G. An updated systematic review and meta-analysis of the prevalence of hepatitis B virus in Ethiopia. BMC Infect Dis. 2019;19(1):917.

Zhao S, Xu Z, Lu Y. A mathematical model of hepatitis B virus transmission and its application for vaccination strategy in china. Int J Epidemiol. 2000 Aug;29(4):744-52. doi: 10.1093/ije/29.4.744. PMID: 10922354.

Zhao, S., Xu, Z. Y, & Lu, Y., (2000). A mathematical model of hepatitis B virus Transmission and its application for vaccination strategy in china.

International Journal of Epidemiology, 29, 744-752. https://www.hepb.org/prevention-and-diagnosis/post-exposure-treatment/

Zhang TL, Li H, Xie N, Fu WH, Wang K, Ding XJ. Mathematical analysis and simulation of a Hepatitis B model with time delay: A case study for Xinjiang, China. Math Biosci Eng. 2019 Dec 13;17(2):1757-1775. doi: 10.3934/mbe.2020092. PMID: 32233606.

Zada, I., Naeem Jan, M., Ali, N. et al. Mathematical analysis of hepatitis B epidemic model with optimal control. Adv Differ Equ 2021, 451 (2021). https://doi.org/10.1186/s13662-021-03607-2

Zhang, J. And Zhang, S.(2018) Application and optimal control for a HBV model with vaccination and treatment. Discrete Dynamics in Nature and society, vol. 2018. Article ID 2076983, 13 pages 208

Zada, I., Muhammad, N. J., Nigar, A., Dala, A., Kattakkaran, S. N. And Gul, Z.(2021) Mathematical Analysis of hepatitis B epidemic Model with optimal control. Advance in Differential Equations.(2021)

Zhang, T., Wang, K., Zhang, X. (2015). Modeling and analysing the transmission Dynamics of HBV epidemiology on Xinjing China. Plos One 10(9): e0138765

Zou L, Zhang W, and Ruan S(2010), Modeling the transmission dynamics and control of hepatitis B virus in China, *Journal of Theoretical Biology*, 2010, **262**: 330–338.

Zou, L. and Zhang, W. ((2009). Modeling the transmission dynamics and control of hepatitis B virus in China. J. Theor. Biol., Vol. 10, pp. 1-9.