Theoretical analysis on the transmission dynamics of HBV Disease with the effect of intervention of vaccination and treatment

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Abstract: In this paper, we formulate a SVEIQR model for the Hepatitis B virus (HBV) using ordinary differential equations. The model is then tested for well posedness by finding the positivity, boundedness and existence of the solution. Then, an approximate analytical solution to the model is obtained by executing the Homotopy Perturbation Method (HPM) which is a coupling of homotopy and perturbation techniques. This solution helps us to study the model dynamically. The validity of the method is checked by using numerical simulation. These results show that HPM is highly reliable in solving such non-linear models. The results are applicable to the entire solution domain.

Keywords: Hepatitis B virus model, Existence and Uniqueness, Homotopy Perturbation Method

1. Introduction

Hepatitis B is viral disease that attacks the liver thereby causing acute and chronic diseases. It is a global health problem putting people’s life at risk by causing complications such as cirrhosis and liver cancer. WHO has estimated that, at present a total of 257 million people live with chronic HBV infection with a higher percentage of illness and death (Hepatitis B Foundation, n.d.). The Transmission of HBV is through the direct contact with an infected person. A major proportion of the transmission is from mother to child during birth or through early childhood transmission and these routes are the major response for a chronic infection. Infection acquired in infancy or early childhood contributes to 95% of chronic cases where as the one acquired during adulthood contributes to 5% of chronic cases worldwide (Hepatitis B, n.d.). The virus causing agent of Hepatitis B is able to survive outside the body for atleast 7 days during which the virus has the ability to still cause infection.

Mathematical modelling of infectious diseases helps in comprehending the dynamics and transmission of the disease and thereby contributing to invention of an
intervention program in overcoming the further outbreak of the disease. Zhang (Zhang, 2018) studied an optimal model of HBV with vaccination and treatments. The vaccination effects were studied by Wiraningsih (Wiraningsih, 2015). In 2017, Beay (Beay, 2017) remodelled it by adding a migration compartment and in 2019, Anji (Aniji, 2019) remodelled it by adding a new compartment called carrier compartment. In 2018, Olajide et al. studied the transmission dynamics and the optimal control under isolation, treatment and vaccination of Hepatitis B Virus.

Motivated by the above works, we proposed a SVEIQR model for Hepatitis B by introducing a new compartment as quarantined. Our choice is driven by the fact that isolating an infected/exposed individual can further aid in reducing the spread of the disease and this model is the first of its kind.

This paper is organised as follows: section 2 presents the SVEIQR model for Hepatitis B, section 3 highlights the basic properties of the model such as positivity, boundedness and existence of the solution to the model, section 4 shows our attempt in finding an approximate analytical expression of the model by employing the technique of Homotopy Perturbation technique and section 5 deals with the numerical stimulation for the solution obtained.

2. Model Formulation

To formulate the model we divide the total population into six compartments namely, the susceptible class, the vaccinated class, the exposed class, the infected class, the quarantined class and the recovered class. The susceptible class denotes the individuals who are prone to the disease and also those who are in close contact with the infected individuals. The vaccinated class represents the individuals who have been vaccinated but still are at the risk of catching the disease under some suitable conditions. The exposed class denotes the individuals who have been exposed to the virus and are at the risk of infection. The infected class denotes the individuals who have been infected by the disease and also those who are able to infect the susceptible class. Since HBV is a serious infectious disease transmitted through direct contact, we have introduced a new class called the quarantined class. The quarantined class represents those individuals (exposed and infected) who are isolated for the risk of further infection. Lastly, the recovered class denotes the individuals who have been recovered from the infection after a period of immunization and treatment.

Figure 1: Schematic Diagram for the SVEIQR model
The following assumptions were made to develop the mathematical model of the disease,

- The population size is assumed to be a constant $N$ i.e. the birth rate is equal to the death rate.
- The new borns are vaccinated at the rate $\alpha$.
- The rate at which the susceptible becomes exposed to the disease is $\nu$.
- The transmission rate from the exposed to the infected class is given by $\eta$.
- The susceptible individuals after taking the vaccine move to recovered class at the rate $\delta$.
- After a period of immunization and treatment the infected class becomes recovered at the rate $\phi$.
- The rate at which the infected and the exposed individuals are isolated/quarantined is given by $\zeta$ and $\theta$.
- The quarantined individuals move to the recovered class at the rate $\sigma$.
- The natural mortality rate is given by $\mu$ whereas the HB induced mortality rate is given by $\beta$.
- The vaccination expiry rate is given by $\phi$.

We represent the mathematical model as

$$
\frac{dS}{dT} = (1 - \alpha)\mu + \phi V + \gamma R - (\mu + \gamma \lambda + \delta)S
$$

(1)

$$
\frac{dV}{dT} = \alpha\mu - (\phi + \mu)V
$$

(2)

$$
\frac{dE}{dT} = \gamma IS - (\eta + \mu + \theta)E
$$

(3)

$$
\frac{dI}{dt} = \eta E - (\mu + \beta + \varphi + \zeta)I
$$

(4)

$$
\frac{dQ}{dt} = \theta E + \xi I - (\mu + \beta + \sigma)Q
$$

(5)

$$
\frac{dR}{dt} = \delta S + \phi I + \sigma Q - (\gamma + \mu)R
$$

(6)

With the initial conditions as

$$S(0) = S_i, \quad V(0) = V_i, \quad E(0) = E_i, \quad I(0) = I_i, \quad Q(0) = Q_i \quad \text{and} \quad R(0) = R_i.$$
Table 1: Parameter values and initial conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Initial Values</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S$</td>
<td>Susceptible Population</td>
<td>0.6</td>
<td>Assumed</td>
</tr>
<tr>
<td>$V$</td>
<td>Vaccinated Population</td>
<td>0.12</td>
<td>Assumed</td>
</tr>
<tr>
<td>$E$</td>
<td>Exposed Population</td>
<td>0.07</td>
<td>Assumed</td>
</tr>
<tr>
<td>$I$</td>
<td>Infected Population</td>
<td>0.04</td>
<td>Assumed</td>
</tr>
<tr>
<td>$Q$</td>
<td>Quarantined Population</td>
<td>0.01</td>
<td>Assumed</td>
</tr>
<tr>
<td>$R$</td>
<td>Recovered Population</td>
<td>0.2</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\mu$</td>
<td>Natural Mortality rate</td>
<td>0.0121</td>
<td>(Kamyad, 2014)</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Immunized New borns</td>
<td>0.005</td>
<td>(Kamyad, 2014)</td>
</tr>
<tr>
<td>$\beta$</td>
<td>HB induced Mortality</td>
<td>0.015</td>
<td>(Kamyad, 2014)</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Transmission rate from S to V</td>
<td>1.5</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Transmission rate from S to R</td>
<td>0.001</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Transmission rate from R to S</td>
<td>0.06</td>
<td>(Kamyad, 2014)</td>
</tr>
<tr>
<td>$\nu$</td>
<td>Transmission rate from S to E</td>
<td>0.08</td>
<td>(Kamyad, 2014)</td>
</tr>
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<td>$\eta$</td>
<td>Transmission rate from E to I</td>
<td>0.5</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\zeta$</td>
<td>Transmission rate from I to Q</td>
<td>0.02</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\theta$</td>
<td>Transmission rate from E to Q</td>
<td>1.08</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>Transmission rate from Q to R</td>
<td>0.05</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\varphi$</td>
<td>Transmission rate from I to R</td>
<td>0.01</td>
<td>(Kamyad, 2014)</td>
</tr>
</tbody>
</table>

3. Basic Properties of the Model

3.1 Positivity of the solution:
Theorem 1: Let the initial data of the model be 
\[ S_i \geq 0, V_i \geq 0, E_i \geq 0, I_i \geq 0, Q_i \geq 0, R_i \geq 0. \]
Then the solutions \( S(t), V(t), E(t), I(t), Q(t), R(t) \) to the eqn (1-6) of the model will remain positive for all time \( t \geq 0 \).

Proof:

Let \( S_i \geq 0, V_i \geq 0, E_i \geq 0, I_i \geq 0, Q_i \geq 0, R_i \geq 0. \)

Assume that all the other parameters are positive.

Consider the first equation:
\[
\frac{dS}{dT} = (1 - \alpha)\mu + \phi V + \gamma R - (\mu + \gamma I + \delta)S
\]

(7)

Clearly, \( \frac{dS}{dT} \geq -(\mu + \gamma I + \delta)S \) which on solving gives \( S(t) \geq S_i e^{-(\mu+\gamma I+\delta)t} \).

Since \( S_i > 0 \) & \( e^{-(\mu+\gamma I+\delta)t} > 0 \), we can conclude that
\( S(t) \geq S_i e^{-(\mu+\gamma I+\delta)t} > 0 \).

Similarly, by carrying out the same procedure we see that \( V(t) > 0, E(t) > 0, I(t) > 0, Q(t) > 0 \) and \( R(t) > 0 \).

Hence proved.

3.2 Boundedness of the solution:

Theorem 2: Suppose the system of eqns (1-6) holds and the feasible solution set of the model with initial conditions \( S_i \geq 0, V_i \geq 0, E_i \geq 0, I_i \geq 0, Q_i \geq 0, R_i \geq 0 \) are satisfied, then is a bounded region.

Proof:

For the model, the total population is denoted by \( N \) and given by
\[
N(t) = S(t) + V(t) + E(t) + I(t) + Q(t) + R(t).
\]

(8)

Substituting the eqns (1-6) in the above equations, we get
\[
\frac{dN}{dt} = (1 - \alpha)\mu - \mu(S + V + E + I + Q + R) - \beta(I + Q)
\]

(9)
In the absence of death due to Hepatitis B (i.e. \( I = 0 \) & \( Q = 0 \)), the above equation becomes
\[
\frac{dN}{dt} \leq (1 - \alpha)\mu - \mu N
\]
(10)

Integrating we get,
\[
N(t) \leq N_i e^{-\mu t} + (1 - \alpha)(1 - e^{-\mu t})
\]
(11)

Taking limit as \( t \to \infty \) in eqn(11) on both sides, we get
\[
\Omega = \{ (S,V,E,I,Q,R) \in \mathbb{R}^6 : 0 \leq N \leq (1 - \alpha) \}
\]

Hence the solution set is positively invariant on both sides.

3.3 Existence and Uniqueness of the solution:

Lemma 3.1: Let \( D \subset \mathbb{R}^n \) and \( f : D \to \mathbb{R} \) be a non-linear vector field. \( f \) is continuous and Lipschitz in \( B = \{ x \in D : \| x - x_0 \| \leq r \} \) for some real \( r \) with \( r > 0 \). Then, there exists some \( \delta > 0 \) such that \( x' = f(t,x), x(t_0) = x_0 \), has some unique solution.

Theorem 3.2: Suppose \( F_i(t,x), x(t_0) = x_0, i = 1,2,3,4,5,6 \) exists and unique in solution. Then the system satisfies Lipschitz condition.

Proof:

It is enough to show that \( \frac{\partial f_i}{\partial t_j} \), \( i, j = 1,2,3,4,5,6 \) are continuous and bounded in \( D \).

Let
\[
f_1 = (1 - \alpha)\mu + \phi V + \gamma R - (\mu + \gamma I + \delta)S
\]
(12)
\[
f_2 = \alpha \mu - (\phi + \mu) V
\]
(13)
\[
f_3 = \gamma S - (\eta + \mu + \theta)E
\]
(14)
\[
f_4 = \eta E - (\mu + \beta + \varphi + \xi)I
\]
(15)
\[
f_5 = \theta E + \xi I - (\mu + \beta + \sigma)Q
\]
(16)
\[
f_6 = \delta S + \varphi I + \sigma Q - (\gamma + \mu)R
\]
(17)
We obtain the partial derivatives of eqn(12-17) as follows

For $f_1$

\[
\left| \frac{\partial f_1}{\partial S} \right| = \gamma S < \infty, \quad \left| \frac{\partial f_1}{\partial E} \right| = \gamma S < \infty, \\
\left| \frac{\partial f_1}{\partial I} \right| = (\mu + \gamma I + \delta) < \infty, \quad \left| \frac{\partial f_1}{\partial V} \right| = \phi < \infty,
\]

(18)

For $f_2$

\[
\left| \frac{\partial f_2}{\partial S} \right| = \left| \frac{\partial f_2}{\partial E} \right| = \left| \frac{\partial f_2}{\partial I} \right| = \left| \frac{\partial f_2}{\partial Q} \right| = \left| \frac{\partial f_2}{\partial R} \right| = 0 < \infty, \\
\left| \frac{\partial f_2}{\partial V} \right| = -(\phi + \mu) < \infty
\]

(19)

For $f_3$

\[
\left| \frac{\partial f_3}{\partial S} \right| = \gamma I < \infty, \quad \left| \frac{\partial f_3}{\partial E} \right| = \gamma S < \infty, \quad \left| \frac{\partial f_3}{\partial I} \right| = (\eta + \mu + \theta) < \infty, \\
\left| \frac{\partial f_3}{\partial V} \right| = \left| \frac{\partial f_3}{\partial Q} \right| = \left| \frac{\partial f_3}{\partial R} \right| = 0 < \infty
\]

(20)

For $f_4$

\[
\left| \frac{\partial f_4}{\partial S} \right| = \left| \frac{\partial f_4}{\partial V} \right| = \left| \frac{\partial f_4}{\partial Q} \right| = \left| \frac{\partial f_4}{\partial R} \right| = 0 < \infty, \\
\left| \frac{\partial f_4}{\partial I} \right| = -(\mu + \beta + \phi + \xi) < \infty, \quad \left| \frac{\partial f_4}{\partial E} \right| = \eta < \infty
\]

(21)

For $f_5$

\[
\left| \frac{\partial f_5}{\partial S} \right| = \left| \frac{\partial f_5}{\partial V} \right| = \left| \frac{\partial f_5}{\partial R} \right| = 0 < \infty,
\]
The partial derivatives exist and are continuous and bounded. Hence the solution for the system exists and is unique.

4. Approximate analytical solution for the Hepatitis B model

Non-linear differential equations play a pivot role in modelling of natural phenomena in science and engineering. The fundamental aim of non-linear differential equations is to find an approximate analytical solution as these solutions are time consuming and complex in nature. Hence, a great deal of focus has been given in finding the solutions of non-linear differential equations. Recently, many authors have applied the Homotopy Perturbation Method (HPM) in solving the non-linear differential equation. It was first introduced by Ji Huan He (He, Homotopy perturbation technique, 1999), (He, 2000), (He, 2003). HPM has then been adopted by various researchers (He, 2005), (Adamu, 2014), (Sivasamy, 2021), (Peter, 2018), (Sivasamy, 2023), in finding the solutions of such non-linear equations in various disciplines. In this paper, we attempt to find the solution of Hepatitis B Virus model by using HPM. Appendix B demonstrates the solving procedure for the non-linear time-dependent differential equations, eqn. (1)-eqn. (6), by using HPM. The obtained results are as follows

\[
S(t) = S_i e^{-(\mu+\delta)t} + \frac{\alpha \phi \beta}{(\phi + \mu)(\mu + \delta)} \left(1 - e^{-(\mu+\delta)t}\right) - \left(\gamma_i - \frac{\alpha \beta}{(\phi + \mu)}\right) \left(\frac{\phi}{\delta - \phi}\right) \left(e^{-(\mu+\phi)t} - e^{-(\mu+\delta)t}\right)
+ \frac{\gamma R_i}{\delta - \gamma} \left(e^{-(\mu+\gamma)t} - e^{-(\mu+\delta)t}\right) + \frac{\gamma A_i S_i}{\mu + \beta + \psi + \xi} \left(e^{-(2\mu+\beta+\psi+\xi+\delta)t} - e^{-(\mu+\delta)t}\right)
\]

(24)

\[
E(t) = E_i e^{-(\mu+\eta+\phi)t} + \frac{\gamma A_i S_i}{\eta + \theta - \delta - \mu - \beta - \psi - \xi} \left(e^{-(2\mu+\beta+\psi+\xi+\delta)t} - e^{-(\eta+\mu+\theta)t}\right)
\]

(25)
\[ I(t) = I_i e^{-(\mu+\beta+\gamma)t} + \frac{\eta E_i}{\beta + \psi + \xi - \eta - \theta} \left( e^{-(\mu+\beta+\psi+\xi)t} + e^{-(\eta+\mu+\theta)t} \right) \]

(26)

\[ Q(t) = e^{-(\mu+\beta+\sigma)t} Q_i + \frac{\gamma E_i e^{-(\eta+\mu+\gamma)t}}{\beta + \sigma - \eta - \gamma} - \frac{\gamma E_i e^{-(\beta+\mu+\sigma)t}}{\beta + \sigma - \eta - \gamma} + \frac{\xi I_i e^{-(\beta+\phi+\xi+\mu)t}}{\sigma - \phi - \xi} - \frac{\xi I_i e^{-(\beta+\sigma+\mu)t}}{\sigma - \phi - \xi} \]

(27)

\[ R(t) = e^{-(\mu+\gamma)t} R_i + \frac{\delta S_i e^{-(\delta+\mu)t}}{\gamma - \delta} - \frac{\delta S_i e^{-(\gamma+\mu)t}}{\gamma - \delta} + \frac{\phi I_i e^{-(\beta+\phi+\xi+\mu)t}}{\gamma - \beta - \phi - \xi} - \frac{\phi I_i e^{-(\gamma+\mu)t}}{\gamma - \beta - \phi - \xi} + \frac{\sigma Q_i e^{-(\beta+\sigma+\mu)t}}{\gamma - \beta - \sigma} \]

(28)

5. Numerical Simulation

The method of Homotopy Perturbation is employed to find a closed-form analytical solution for the model equations (1-6). The basic idea of HPM is explained in brief in appendix A and the solutions for the eqns. (1-6) are given in the appendix B below. The numerical simulation is carried out in the MATLAB software by using the ode45 function. The validity of the above method is checked by a graphical comparison between the analytical and numerical solutions and this is illustrated in the figures 1-13.

5.1: Results and Discussion:
**Figure 1:** Plot of Susceptible class $S(t)$ against time $t$ for the eqn (1).

**Figure 2:** Plot of Susceptible class $S(t)$ against time $t$ for the eqn (1).

**Figure 3:** Plot of Susceptible class $S(t)$ against time $t$ for the eqn (1).

**Figure 4:** Plot of Vaccinated class $V(t)$ against time $t$ for the eqn (2).

**Figure 5:** Plot of Exposed class $E(t)$ against time $t$ for the eqn (3).

**Figure 6:** Plot of Exposed class $E(t)$ against time $t$ for the eqn (3).
Figure 7: Plot of Exposed class $E(t)$ against time $t$ for the eqn(3).

Figure 8: Plot of Infected class $I(t)$ against time $t$ for the eqn(4).

Figure 9: Plot of Infected class $I(t)$ against time $t$ for the eqn(4).

Figure 10: Plot of Quarantined class $Q(t)$ against time $t$ for the eqn(5).

Figure 11: Plot of Quarantined class $Q(t)$ against time $t$ for the eqn(5).

Figure 12: Plot of Quarantined class $Q(t)$ against time $t$ for the eqn(5).
Figure 13: Plot of Recovered class $R(t)$ against time $t$ for the eqn(6).

Fig. (1-3) presents the plot of susceptible class $S(t)$ against time $t$ for the eqn. (1) by varying and fixing some model parameters. Fig.1 illustrates the population of susceptible class $S(t)$ against time $t$ by varying the parameters $a, \gamma, \delta$. It can be inferred that the rate at which the susceptible cells grow decreases with increasing value of $a$ with time. Fig. 2 depicts the plot of susceptible population $S(t)$ against time $t$ computed using eqn. (1) by varying the parameters $\gamma, \mu, \varphi$. It can be noted that the population increases with increase in values of $\gamma, \varphi$. Fig.3 represents the plot of susceptible population $S(t)$ against time $t$ computed using eqn.(2.1) by varying the parameters $\nu, \psi, \xi$. It can be seen that when $\psi$ and $\xi$ increases and $\nu$ decreases there is a decline in the growth of susceptible cells.

Fig. 4 presents the plot of population vaccinated class $V(t)$ against time $t$ for the eqn. (2) by varying and fixing some model parameters. From the figure it can be inferred that the parameter $\psi$ has a positive impact on the vaccinated population whereas the parameters $a$ and $\mu$ has a negative impact on the vaccinated population. i.e. when $\psi$ decreases, vaccinated population increases and when $a$ and $\mu$ increases the vaccinated population decreases.

Fig. (5-7) presents the plot of population of exposed class $E(t)$ against time $t$ computed using eqn. (3) by varying and fixing some model parameters. Fig. 5 represents the population of exposed class $E(t)$ by varying the parameters. It can be seen that the exposed population decreases with increase in time when the model parameters are increasing. Fig. 6 depicts the population of exposed class $E(t)$ by varying the parameters. It can be noted that the population of exposed class decreases with increase in time when we increase the value of and decrease the value of $\beta, \mu, \psi$. Fig. 7 illustrates the population of exposed class $E(t)$ by varying the parameters. It can be inferred that there is a steady decline in the exposed class population with time.

Fig. (8-9) presents the plot of infected population $I(t)$ against time $t$ derived using the eqn (4) by varying and fixing some parameters. Fig. 8 depicts the infected population $I(t)$ against time $t$ by varying the parameter $\beta, \mu, 0, \xi$. It can be noted that the infected population decreases with time. Fig. 9 illustrates the infected class population $I(t)$ against time $t$ by varying the parameters $\beta, \eta, \psi$. It can be seen that initially the population increases and then gradually decreases and reaches the steady state.

Fig. (10-12) presents the plot of quarantined class $Q(t)$ population against time $t$ by using eqn. (5) by varying and fixing some model parameters. Fig. 10 represents the plot of quarantined class $Q(t)$ population by varying the parameters $\beta, \mu, \xi$ against time $t$. It can be inferred that an initial rise in the quarantined population gradually decreases and reaches
the steady state. Fig. 11 is the plot of quarantined population $Q(t)$ against time by varying the parameters $\mu, \sigma$. It can be noted that there is a steady decline in the quarantined population with increase in time. Fig. 12 illustrates the plot of quarantined population $Q(t)$ against time $t$ by varying the parameters $\theta, \eta, \psi$. It can be seen that there is an exponential decline in the population with time.

Fig. (13) presents the plot of recovered population $R(t)$ computed using eqn. (6) by varying and fixing some model parameters. It can be inferred that when time increases the count of recovered person decreases.

6. Conclusion

In this paper, we have analysed the model of Hepatitis B virus. In order to prevent the further spread of the disease, a new compartment called the quarantined class has been added to the model. The model is then analysed for the positivity and boundedness of the solution. As our prime objective is to find an analytical solution to the non-linear time dependent model, the existence of solution for the model is established. Further, a closed from analytical solution for the model is derived by executing the technique of Homotopy Perturbation Method, a semi-analytical method for finding the solutions of non-linear systems. The validity of the method is then tested by performing the numerical simulation with the graphical comparison of the numerical and analytical results. The correlation between the state variables and the model parameters is also established by the numerical simulation. These results validate the fact that HPM can indeed be adopted for solving the Hepatitis model.

References


