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Optimal control analysis applied to the transmission dynamics of Hepatitis B to primary liver cancer

Opeyemi Odetunde [1], Omoniyi Emmanuel Francis [2,*] and Tunde Solomon Alesinloye [3]

[1] *Department of Mathematics, University of Ilorin, Ilorin, Kwara State, Nigeria.*
[2] *Department of Mathematics, University of Alabama, Birmingham, AL, USA.*
[3] *Department of Mathematics, University of North Dakota, Grand Forks, ND, USA.*

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Abstract

Infection with hepatitis virus, especially hepatitis B virus causes an irritation to the liver. Ranked among the top ten diseases with high mortality rate, viral hepatitis poses a great health challenges worldwide, with threat to chronic infection, hepatitis-related liver cancer and cirrhosis. Hence, a mathematical model to study the dynamics of hepatitis B virus infection from progressing into primary liver cancer was developed for analysis. We aimed at obtaining the optimal control strategies needed to reduce the number of new cases of this disease, and also reducing the deterioration rate of people living with this disease from sliding into primary liver cancer. We introduced four distinct control variables at each point in the model, and assumed that all the controls are set of Lebesque Measurable functions. The Pontryagin's maximum principle (PMP) is employed to establish the optimal effect of these controls on the disease under study. Existence of model solution was established using the appropriate theorem. The model with control strategies was analytically solved using PMP and numerically simulated for each compartments, to establish the effect of the control variables on the dynamics of transmission of this infection within the compartment, and their overall effect on the entire population. Differential transform method (DTM) was later adopted as a semi-analytic scheme to solve the developed model. The series solution of DTM was numerically plotted for each compartment and compared with Runge-Kutta order 4 (RK4) numerical scheme. Analysis of the model with control pinpoint the importance of sensitization and vaccination on the overall dynamics of the infection, while the numerical plot of DTM and RK4 established the efficacy of the adopted semi-analytic method (DTM) to accurately solve the system of equations of the model.

Keywords: 0ptimal control; Lebesque; PMP; DTM; RK4

1. Introduction

Hepatitis, an inflammation of the liver caused by several infectious viruses and noninfectious agents can lead to wide range of health problems, some of which can be fatal. Inflammation is coined from Latin word "inflammatio" which translates to "part of the biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants" (Wikipedia). According to studies, there exist five strains of hepatitis, labelled A, B, C, D and E with each differing in the mode of transmissions, severity, and geographical location but all resulted in liver disease. Incidentally, B and C are the most common, most chronic and most fatal of all the strains, with both of them contributing to more than 60% of all cases worldwide. According to World Health Organization (WHO), hundreds of million individuals worldwide currently live with hepatitis B or C, and needless to say that majority among these people do not have access to effective testing and treatment (WHO, 2024). Hepatitis B can both be chronic or acute, and it is caused by the hepatitis B virus. Transmission dynamics of HBV includes perinatal, blood and bodily fluid contact, no clinical symptoms will be manifested in newly infected and people with acute stage characterized by dark urine, vomiting etc. This disease have

* Corresponding author: Omoniyi Emmanuel Francis

high mortality rate at chronic stage with over a million death (largely due to cirrhosis and primary liver cancer; also known as hepatocellular carcinoma) recorded in year 2022 alone, and it can be prevented with vaccine that is both safe, effective and available (WHO, 2024).

Mathematical modeling of an infectious disease helps mathematician to study and analyzed the pattern of an emerging infection, understand the dynamics of such disease and predict the best approach of eradicating its menace. It is the transformation of an infection-epidemiology into mathematical expression so that analysis can be done for accurate assertion on method of solution. Several mathematical models on HBV exist in literature, with each model being specific about its aim. Xu *et al.,*(2023) analyzed a model to study the effects of vaccination strategies in China against Hepatitis B virus infections. Their analysis showed that to achieve a good result against HBV, a more robust mechanism of prevention and control is required to increase the vaccination of different age groups, and there is the need to sensitize the public to take adequate preventive measures against been infected. Wodajo *et al.,* (2023) also presented a model on the effectiveness of intervention strategies against the spread of HBV by considering the role of vaccinations in their study. They performed the sensitivity analysis of their model parameters against the basic reproduction number, and their study revealed that screening, sensitization and vaccination are important approaches to reduce the pandemicity of HBV. Liang *et al.,* (2018) presented a review of several mathematical models on immunization strategies against HBV transmission. They analyzed the parameters involved in various mathematical models from the year 1994 – 2015, and they concluded that the more closely the parameters considered in the model reflects the dynamics of the disease, the better the usefulness of the result of the model. Malede *et al.,* (2023) discussed the optimal control and cost effectiveness analysis of HB disease, by considering a model with two dosages of vaccine. They obtained the two equilibrium positions for their model and also performed sensitivity analysis of the model parameters with respect to the effective reproduction number. The result obtained from their analyses indicated that control strategies against the spread of the disease is cost effective than treatment.

2. Material and methods

Having considered several models and their analysis, we present a mathematical model of staged progression of HB disease to primary liver cancer (PLC) by stratifying total human population, N, into six epidemiological classes denoted as *M-Partially immune from/after birth, S-Susceptible, E-Exposed, I_1-HB acute stage, I_2-PLC stage and R-removed compartment* respectively (M-S-E-I_1 -I_2 –R). B denotes the birth rate into M-class with immunity obtained from birth through vaccination or other means, δ denotes immunity loss and μ denotes natural mortality rate, which occurs at constant rate for the whole compartments. Other recruitments are taking as immigrants, with total immigrants denoted by π. Recruitment into S-class is at k and into I_1-class at x such that $x + k = 1$. β denotes the incidence rate of new infection, which occurs when the susceptible come in contact with the infectious through any mode of transmissions. Due to incubation period of the disease, freshly infected individual stays in E-class until they begins to show clinical symptoms and then transferred to I_1-class at the rate ϵ. Untested, undetected and untreated individual in I_1 moved to I_2-class at the rate ϑ, and disease induced death occurred in both I_1, I_2 classes at the rate ω_1, ω_2 respectively. Detected I_1, I_2 are removed at the rate σ_1, σ_2 respectively.

2.1. Model Assumptions

Some of the basic assumptions of the model includes:

- Total recruitment is divided into two, birth within the population and recruitment through immigration, thus immigrants are either assumed susceptible of infectious.
- Compartment (I_2) does not contribute to HB epidemic because we assumed it is a result of chronic Hepatitis B left untreated.
- It was assumed mathematically that all model parameters are non-negative

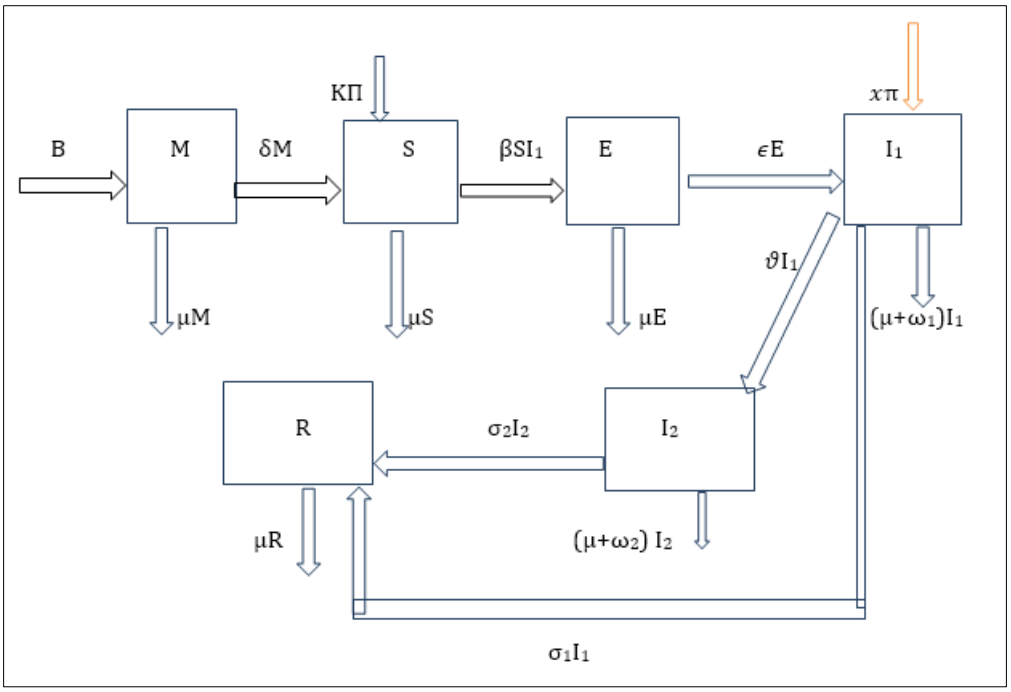

Figure 1 Model flow diagram

The model equations

$$\frac{dM}{dt} = B - (\mu + \delta)M$$

$$\frac{dS}{dt} = k\pi + \delta M - \beta S I_1 - \mu S$$

$$\frac{dE}{dt} = \beta S I_1 - (\mu + \epsilon)E \qquad \ldots\ldots\ldots\ldots\ldots (1)$$

$$\frac{dI_1}{dt} = x\pi I_1 + \epsilon E - (\vartheta + \mu + \omega_1 + \sigma_1)I_1$$

$$\frac{dI_2}{dt} = \vartheta I_1 - (\mu + \omega_2 + \sigma_2)I_2$$

$$\frac{dR}{dt} = \sigma_1 I_1 + \sigma_2 I_2 - \mu R$$

2.2. Qualitative Analysis of the biological model

First, we established the existence and uniqueness of solution to the above biological model using the Lipschitz criteria as adopted by several researchers by finding the partial derivatives of each equation in the system of equations governing the model with respect to each state variable. Suppose $f_1 = \frac{dM}{dt}, f_2 = \frac{dS}{dt}, f_3 = \frac{dE}{dt}, etc.$ in equation (1), then

$\left|\frac{\partial f_1}{dM}\right| = |-(\mu + \delta)| < \infty, \left|\frac{\partial f_1}{dS}\right| = \left|\frac{\partial f_1}{dE}\right| = \left|\frac{\partial f_1}{dI_1}\right| = \left|\frac{\partial f_1}{dI_2}\right| = \left|\frac{\partial f_1}{dR}\right| = 0 < \infty; \left|\frac{\partial f_2}{dM}\right| = \delta, \left|\frac{\partial f_2}{dS}\right| = |-\beta I_1 - \mu| < \infty, \left|\frac{\partial f_2}{dI_1}\right| = |-\beta S| < \infty, \left|\frac{\partial f_2}{dE}\right| = \left|\frac{\partial f_2}{dI_2}\right| = \left|\frac{\partial f_2}{dR}\right| = 0 < \infty; etc.$

Since the partial derivative of each functions exist with respect to the state variables, and are both continuous and bounded, then the system of equations in (1) have a unique solution. Further analysis of the qualitative properties are done in Odetunde and Ibrahim (2016). The basic reproduction number of the model as obtained by Odetunde and Ibrahim (2016) is given as:

$$R_0 = \frac{\epsilon\beta S^0}{(\mu+\epsilon)(\vartheta+\mu+\omega_1+\sigma_1-x\pi)} \quad \ldots\ldots\ldots(2)$$

2.3. Optimal Control Analysis of the Model

The control $u_1(t)$ where $0 \le u_1 \ll 1$ deals with partial immunity obtained at birth by an infant as a result of vaccination of its pregnant mother or during immunization at birth. If this immunity can be permanent, it implies that such categories of infant will never be infectious in their lifetime. For this to occur, the vaccine dosage and its content must be analyzed and improved to give optimum protection that can guarantee permanent immunity.

The control $u_2(t), 0 \le u_2 \le 1,$ models the effort needed in reducing the number of infective/exposed by proper sensitization of sexually active populations against sleeping with an HBV infected patients. The third control $u_3(t)$, for $0 \le u_3 \ll 1$ deals with the percentage of susceptible individuals vaccinated per unit of time. The last control $u_4(t)$ for $0 \le u_4 \ll 1$, measured the effect of HBV therapeutic treatment measure on the reduction rate of HBV patients being transmitted to Primary Liver Cancer patients.

The objective is to minimize the number of HBV infected cases in a population with large susceptible to infected ratio and also to minimize the deterioration rate of HBV to Primary Liver Cancer among the infected population while maintaining the cost associated to control u_1, u_2, u_3 and u_4.

Our state system is the following system of differential equations that model the dynamics of the HBV transmission rate to Primary Liver Cancer and the control parameters.

$$\frac{dM}{dt} = (1-u_1)B - (\mu+\delta)M$$

$$\frac{dS}{dt} = k\pi + \delta M - (1-u_2)\beta S I_1 - \mu S + u_3 S$$

$$\frac{dE}{dt} = (1-u_2)\beta S I_1 - (\mu+\epsilon)E \quad \ldots\ldots\ldots(3)$$

$$\frac{dI_1}{dt} = x\pi I_1 + \epsilon E - (\vartheta+\mu+\omega_1+\sigma_1)I_1 + u_4 I_1$$

$$\frac{dI_2}{dt} = \vartheta I_1 - (\mu+\omega_2+\sigma_2)I_2$$

$$\frac{dR}{dt} = \sigma_1 I_1 + \sigma_2 I_2 - \mu R$$

With initial conditions

$$M(0) = M_0;\ S(0) = S_0;\ E(0) = E_0;\ I_1(0) = I_{10};\ I_2(0) = I_{20};\ R(0) = R_0 \quad \ldots\ldots\ldots(4)$$

The proposed cost functional is expressed as:

$$J(u_1,u_2,u_3,u_4) = \int_{t_0}^{t_f}\left\{M(t)+S(t)+I_1(t)+\frac{k_1}{2}u_1^2+\frac{k_2}{2}u_2^2+\frac{k_3}{2}u_3^2+\frac{k_4}{2}u_4^2\right\}dt \quad \ldots\ldots\ldots(5)$$

Where k_1, k_2, k_3 and k_4 are the weighting constants for the mass vaccination of pregnant mothers, mass sensitization of sexually active population against HBV transmission, mass vaccination of susceptible class and mass treatment of HBV infected class respectively.

The objective of the proposed optimal control problem is to maximize the target population of immune individual against HBV at a given final time t_f while minimizing the cost associated with effective vaccination, sensitization and therapeutic treatment available. Hence, we assume a cost associated with effective vaccination, sensitization program and therapeutic treatment to be quadratic functions.

We take into account the objective functional (5) derived to model (2). Pontryagins' Maximum Principle (PMP) will be employed to determine the optimal control u_1, u_2, u_3 and u_4 with associated conditions as given in (4). The PMP changes (5), (3) and (4) into a problem of minimizing pointwise a Hamiltonian H, with respect to (u_1, u_2, u_3, u_4) simply as:

$$H(M,S,E,I_1,I_2,R,u_1,u_2,u_3,u_4,\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,\lambda_6) = M(t) + S(t) + I_1(t) + \frac{k_1}{2}u_1^2 + \frac{k_2}{2}u_2^2 + \frac{k_3}{2}u_3^2 + \frac{k_4}{2}u_4^2 + \lambda_1\frac{dM}{dt} + \lambda_2\frac{dS}{dt} + \lambda_3\frac{dE}{dt} + \lambda_4\frac{dI_1}{dt} + \lambda_5\frac{dI_2}{dt} + \lambda_6\frac{dR}{dt} \quad \text{…….. (6)}$$

Where the set of controls

$$U = \{u: [t_0, t_f] \to [0,1] |\ u \ is \ Lebesque \ Measurable\}$$

Re-writing (6) by making use of (3), we have:

$$H = M + S + I_1 + \frac{k_1}{2}u_1^2 + \frac{k_2}{2}u_2^2 + \frac{k_3}{2}u_3^2 + \frac{k_4}{2}u_4^2 + \lambda_1[(1-u_1)B - (\mu+\delta)M] + \lambda_2[k\pi + \delta M - (1-u_2)\beta S I_1 - \mu S + u_3 S] + \lambda_3[(1-u_2)\beta S I_1 - (\mu+\epsilon)E] + \lambda_4[x\pi I_1 + \epsilon E - (\vartheta + \mu + \omega_1 + \sigma_1)I_1 + u_4 I_1] + \lambda_5[\vartheta I_1 - (\mu + \omega_2 + \sigma_2)I_2] + \lambda_6[\sigma_1 I_1 + \sigma_2 I_2 - \mu R] \quad \text{…….. (7)}$$

Having formed the Hamiltonian, we want to test for the optimal control $(u_1^*, u_2^*, u_3^*, u_4^*)$ that minimizes $J(u_1, u_2, u_3, u_4)$ over the invariant region which can be obtained from:

Optimality condition: $\frac{\partial H}{\partial u_i} = 0$, for i = 1,2,3,4

Adjoint functions $\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial x_i}$, i = 1,2, ... ,6

And x_i represent equations corresponding to the state variables.

To characterize the optimal control using PMP, we obtained the adjoint equations using $\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial x_i}$

Hence,

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial M} = -\left[1 + \lambda_1\left(-(\mu+\delta)\right) + \delta\lambda_2\right] \quad \text{…….. (8)}$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial S} = -\left[1 + \lambda_2\left((1-u_2)\beta I_1 - \mu + u_3\right) + \lambda_3(1-u_2)\beta I_1\right] \text{……. (9)}$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial E} = -[\lambda_3[-(\mu+\epsilon)] + \lambda_4\epsilon] \quad \text{…….. (10)}$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_1} = -[1 + \lambda_2[-(1-u_2)\beta S] + \lambda_3(1-u_2)\beta S + \lambda_4[x\pi - (\vartheta + \mu + \omega_1 + \sigma_1) + u_4] + \lambda_5\vartheta + \lambda_6\sigma_1] \text{…… (11)}$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial I_2} = -[\lambda_5[-(\mu + \omega_2 + \sigma_2)] + \lambda_6\sigma_2] \quad \text{…….. (12)}$$

$$\frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial R} = \lambda_6\mu \quad \text{…….. (13)}$$

From (13):

$$\frac{d\lambda_6}{dt} = \lambda_6\mu$$

$$\int \frac{d\lambda_6}{\lambda_6} = \int \mu dt$$

$$\lambda_6(t) = c_6 e^{\mu t} \quad \text{…….. (14)}$$

From (12):

$$\frac{d\lambda_5}{dt} = \lambda_5(\mu + \omega_2 + \sigma_2) - \lambda_6\sigma_2$$

$$\frac{d\lambda_5}{dt} - \lambda_5(\mu + \omega_2 + \sigma_2) = -\sigma_2 c_6 e^{\mu t}$$

Integrating factor for the above expression is given as: $e^{-(\mu+\omega_2+\sigma_2)t}$

Hence,

$$\lambda_5(t) = e^{(\mu+\omega_2+\sigma_2)t}\left\{\int -\sigma_2 c_6\, e^{-(\omega_2+\sigma_2)t}dt + c_5\right\}$$

With transversality conditions: $\lambda_i(t_f) = 0, \quad i = 1, \ldots, 6$

Next, the characterization of the optimal control is computed on the set $\{t:\ 0 < u^*(t) < 1\}$, as:

$$\frac{\partial H}{\partial u_1} = k_1 u_1 - \lambda_1 B = 0, at\ u_1^*(t)$$

$$\Longrightarrow\ u_1^*(t) = \frac{\lambda_1 B}{k_1}$$

When $\frac{\partial H}{\partial u_1} < 0\ at\ t$, then $u_1^*(t) = 0$, and

$$\frac{\lambda_1 B}{k_1} < 0$$

When $\frac{\partial H}{\partial u_1} > 0\ at\ t$, then $u_1^*(t) = 1$, and

$$\frac{\lambda_1 B}{k_1} > 1$$

So, the characterization of the optimal control $u_1^*(t)$ is thus given as:

$$u_1^*(t) = min\left\{1, max\left\{\frac{\lambda_1 B}{k_1}, 0\right\}\right\}$$

Similarly for control u_2

$$\frac{\partial H}{\partial u_2} = k_2 u_2 - \lambda_2 \beta S I_1 - \lambda_3 \beta S I_1 = 0, \text{at}\ u_2^*(t)$$

$$u_2^*(t) = \frac{(\lambda_2 + \lambda_3)}{k_2}\beta S I_1$$

So, the characterization of the optimal control $u_2^*(t)$ is thus given as:

$$u_2^*(t) = min\left\{1, max\left\{\frac{(\lambda_2 + \lambda_3)}{k_2}\beta S I_1, 0\right\}\right\}$$

Also, for control u_3

$$\frac{\partial H}{\partial u_3} = k_3 u_3 - \lambda_2 S = 0, \text{at } u_3^*(t)$$

$$u_3^*(t) = \frac{\lambda_2 S}{k_3}$$

So, the characterization of the optimal control $u_3^*(t)$ is thus given as:

$$u_3^*(t) = min\left\{1, max\left\{\frac{\lambda_2 S}{k_3}, 0\right\}\right\}$$

Lastly, for control u_4

$$\frac{\partial H}{\partial u_4} = k_4 u_4 - \lambda_4 I_1 = 0 \text{ at } u_4^*(t)$$

$$u_4^*(t) = \frac{\lambda_4 I_1}{k_4}$$

So, the characterization of the optimal control $u_4^*(t)$ is thus given as:

$$u_4^*(t) = min\left\{1, max\left\{\frac{\lambda_4 I_1}{k_4}, 0\right\}\right\}$$

2.4. Numerical Simulation of the control Model

In this section, we present the numerical simulation of the optimal control analysis of the model using Adams-Bashford predictor-corrector approach.

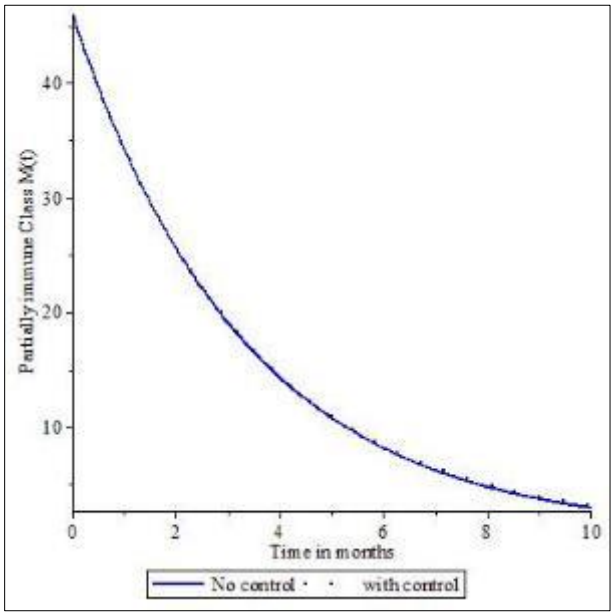

Figure 2 Plot of M-class for both controlled and uncontrolled Models

The graph in figure 2 established no deviation in both models, with or without control, the change in the M-class remain unaffected. This implies that the control introduced to this compartment has little to no overall effect on population changes of this group of people. The simplest explanation for this scenario is that, there is absolutely no vaccine that can efficiently protect the immune system of an individual from variants of organisms causing the illness.

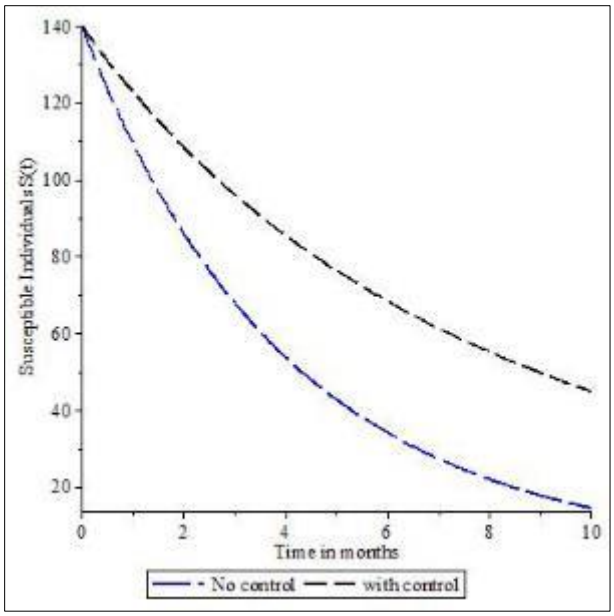

Figure 3 Plot of S-class for both controlled and uncontrolled Models

In figure 4, the population change for S-class is presented with and without the control. Two controls were introduced into this compartment in a bid to educate the populace about HBV and to establish the importance of sensitization and vaccination in reducing the spread. In the absence of these controls, the population of the susceptible reduces faster than when the controls were implemented. This ascertained that, depending on the success rate of our controls, the population of the susceptible individual can be maintained steadily over a longer period of time. Without the control, all susceptible individuals will have a contact with the disease within their lifespan, because the numerical value of the repoduction number in equation (2) is greater than unity.

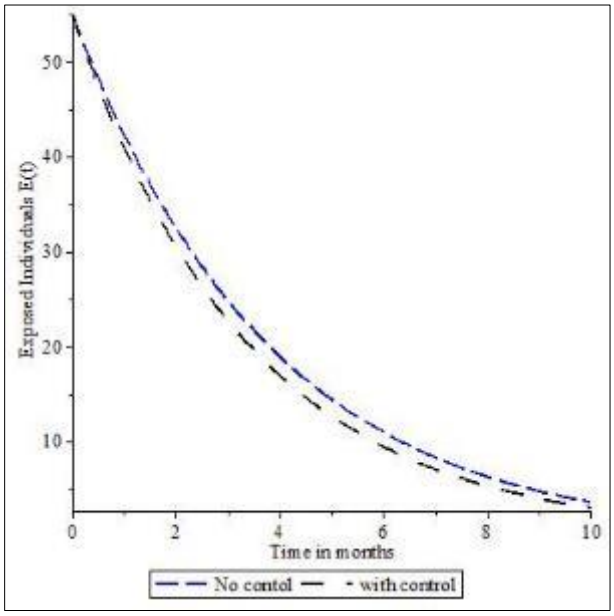

Figure 4 Plot of M-class for both controlled and uncontrolled Models

There is rapid depletion in population of exposed compartment with control implemented as depicted in figure 4. This is due to the fact that there is a reduce rate of contact with the disease as a result of the controls implemented in the S-class. Without the control, exposed population was emptied into the infectious class at a steady rate. In figures 5 and 6, the dynamics of population change for both I_1, I_2 classes are displayed respectively for both the controlled model and the model without control. It is evident from figure 5 that without the introduction of effective treatment strategy (u_4) for HBV, the deterioration rate of HBV patient to liver cirrhosis (primary liver cancer) is at a higher rate. With the

control, the population of the HBV class decreases minimally. This implies that at $u_4 \leq 0.5$ (the value used to plot the graph), the effect of the control strategy introduced does not guaranteed total recovery of infected. Hence, improving the quality of the therapeutic treatment for HBV can have significant positive influence on the overall standard of living of the infectious, thereby reducing the number of PLC that may arise from them. In figure 6, there is little differences in the two graphs for both the model with control and without control. This can be traced to the fact that liver damage can hardly be undone, although further can be minimized with effective strategies. Figure 7 is that of the recovered class with and without control. Since no control was implemented on that particular group of people, the slight differences between both graphs is traceable to earlier control on the I_1 −class.

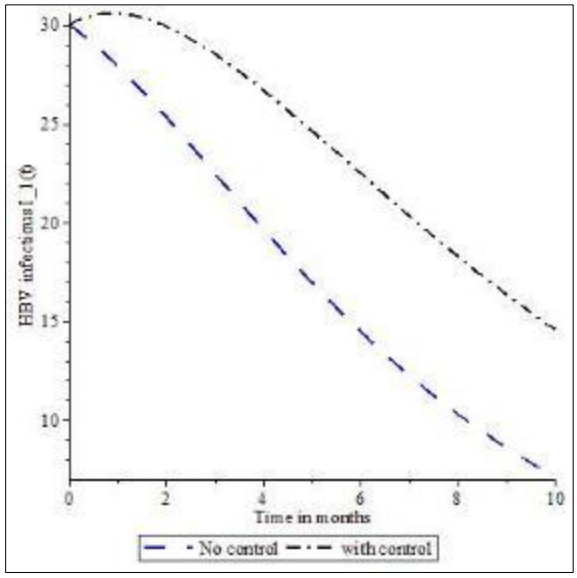

Figure 5 Plot of HBV-class for both controlled and uncontrolled Models

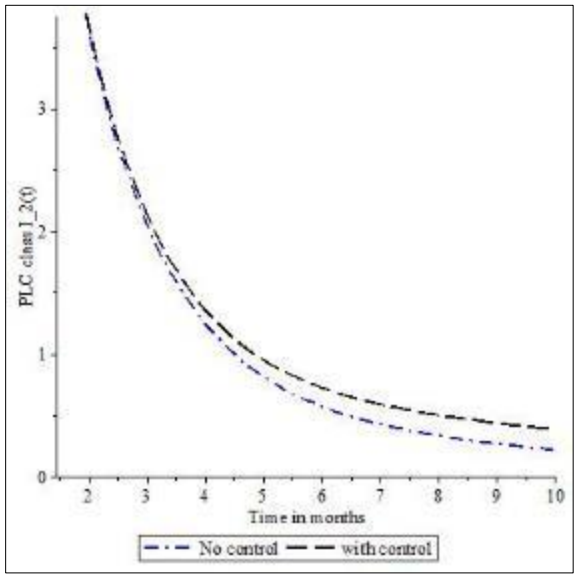

Figure 6 Plot of PLC-class for both controlled and uncontrolled Models

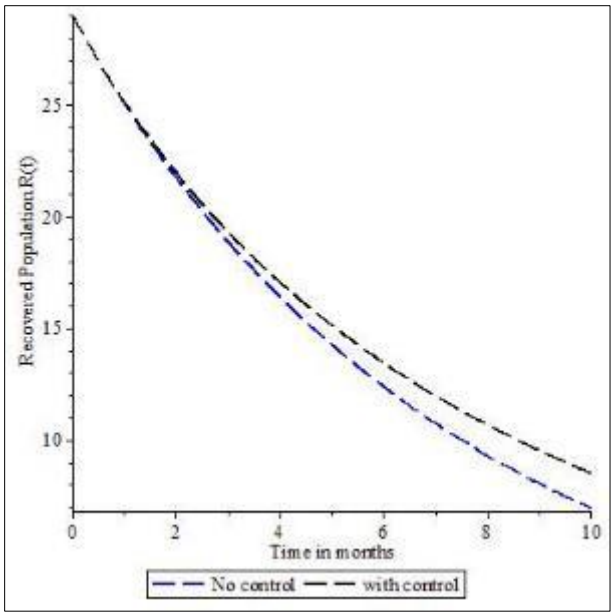

Figure 7 Plot of R-class for both controlled and uncontrolled Models

2.5. Semi-Analytic Solution of the Model

Due to nonlinear nature of some of the equations governing the model, a semi-analytic method of solution was applied, in order to get a series solution. Among the well-established semi-analytic method with great accuracy at solving nonlinear differential equations is differential transform method. This method has been adopted by various researcher, such as Akinboro *et al.,* (2014), Odetunde *et al.,* (2021), Olajide (2020) and Odetunde (2021) among others. This method involves transforming the system of equation (1) into a series form, by using DTM operational properties. These properties are well-defined and clearly stated in tabular form in Akinboro *et al.,* (2014) and Odetunde *et al.,* (2021). Adopting these properties on system in equation (1), the DTM equivalent of the model equations is given as:

$$M(j+1) = \frac{1}{j+1}[B - (\mu+\delta)M(j)]$$

$$S(j+1) = \frac{1}{j+1}[k\pi + \delta M(j) - \beta \sum_{l}^{j} S(l)I_1(j-l) - \mu S(j)]$$

$$E(j+1) = \tfrac{1}{j+1}\left[\beta \textstyle\sum_{l}^{j} S(l)I_1(j-l) - (\mu+\epsilon)E(j)\right] \quad \text{..... (15)}$$

$$I_1(j+1) = \frac{1}{j+1}[x\pi I_1(j) + \epsilon E(j) - (\vartheta+\mu+\omega_1+\sigma_1)I_1(j)]$$

$$I_2(j+1) = \frac{1}{j+1}[\vartheta I_1(j) - (\mu+\omega_2+\sigma_2)I_2(j)]$$

$$R(j+1) = \frac{1}{j+1}[\sigma_1 I_1(j) + \sigma_2 I_2(j) - \mu R(j)]$$

Using parameter values in Table 1 together with an assumed initial values of M(0) := 46; S(0) := 140; E(0) := 55; $I_1(0)$:= 30; $I_2(0)$:= 13; R(0) := 29, the following series solution of (15) was obtained

$$M(t) := 46 - 13.6 * t + 2.040000000\, t^2 - 0.2040000000\, t^3 + O(t \geq 4)$$

$$S(t) := 140 - 34.432930 * t + 4.438803475\, t^2 - 0.3832439580\, t^3 + O(t \geq 4)$$

$$E(t) := 55 - 14.4000 * t + 1.844489525\, t^2 - 0.1651252261\, t^3 + O(t \geq 4) \text{ ..... (16)}$$

$$I_1(t) := 30 - 1.636100 * t - .5254104465 * t^2 + .1031427785 * t^3 + O(t \geq 4)$$

$$I_2(t) = 13 - 8.663 * t + 3.024110750\, t^2 - 0.7092609310\, t^3 + O(t \geq 4)$$

$$Rt := 29 - 4.287 * t + 0.3834660000\, t^2 - 0.03331320386\, t^3 + O(t \geq 4)$$

The graphical plot of (16) is given as:

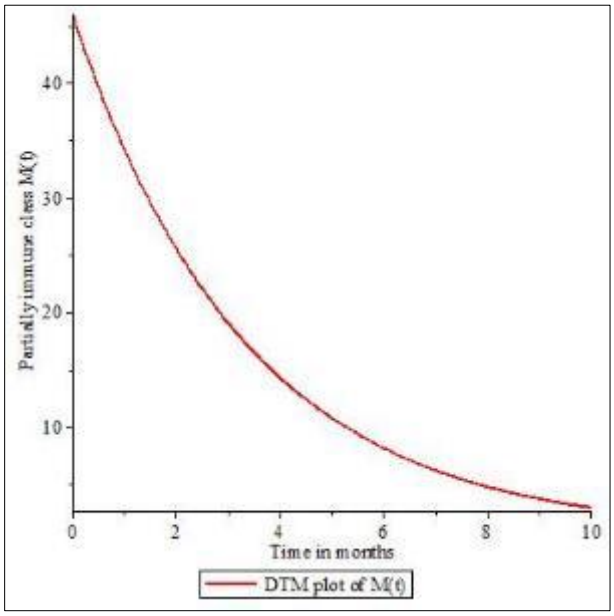

Figure 8 DTM plot of $\boldsymbol{M(t)}$

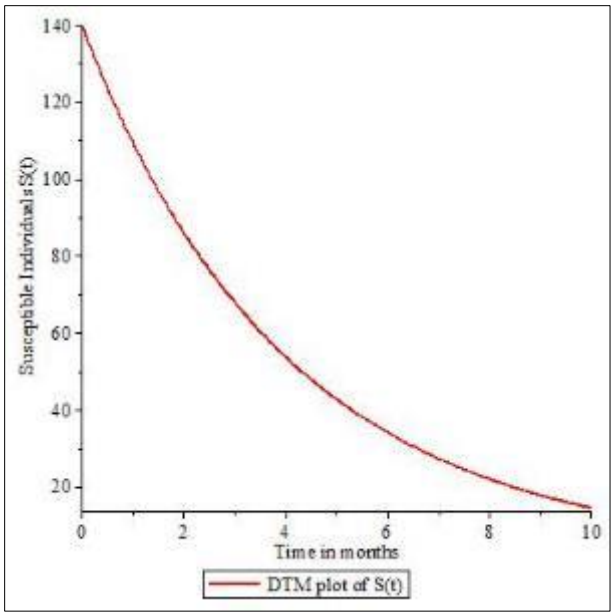

Figure 9 DTM plot of $\boldsymbol{S(t)}$

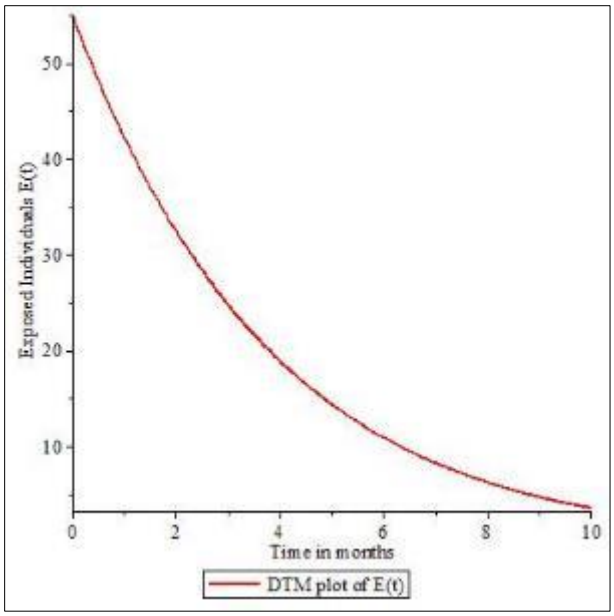

Figure 10 DTM plot of $\boldsymbol{E(t)}$

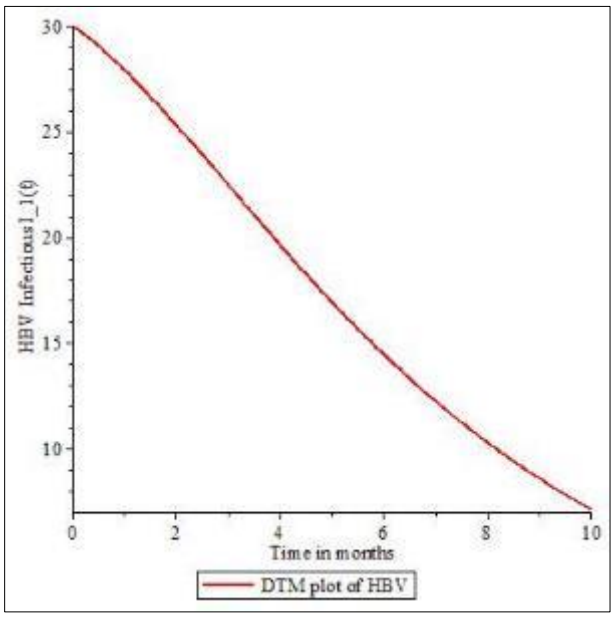

Figure 11 DTM plot of $\boldsymbol{I_1(t)}$

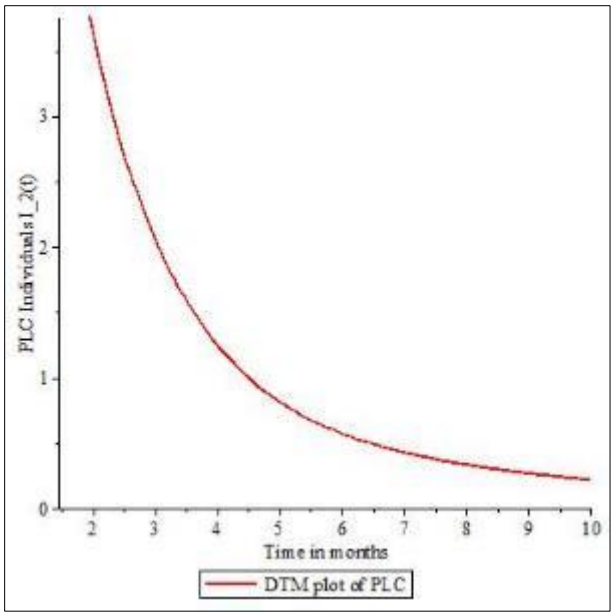

Figure 12 DTM plot of $\boldsymbol{I_2(t)}$

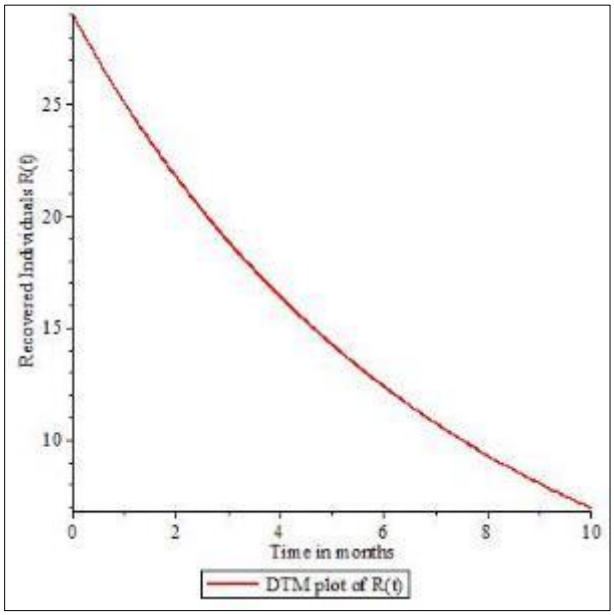

Figure 13 DTM plot of R($\boldsymbol{t}$)

2.6. Numerical Comparison of DTM with Runge-Kutta 4

To establish the accuracy of DTM and its convergence interval, we plot the DTM solution and RK4 of the model for comparison. The numerical solution of RK4 was not explicitly presented but was graphically displayed.

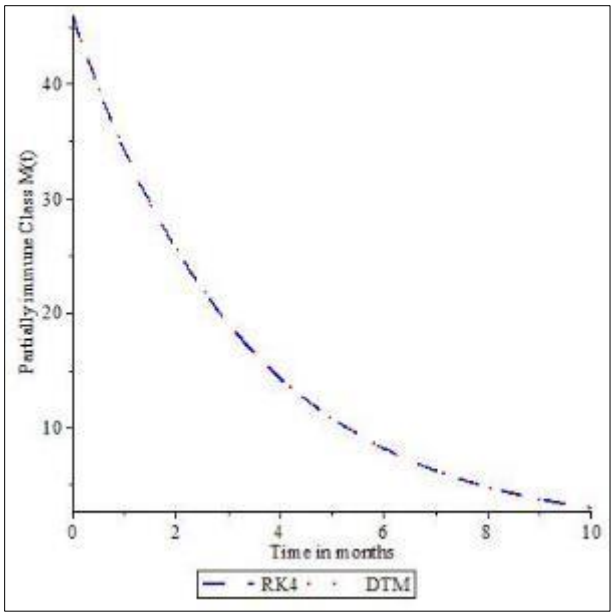

Figure 14 Comparison Plot for $\boldsymbol{M(t)}$

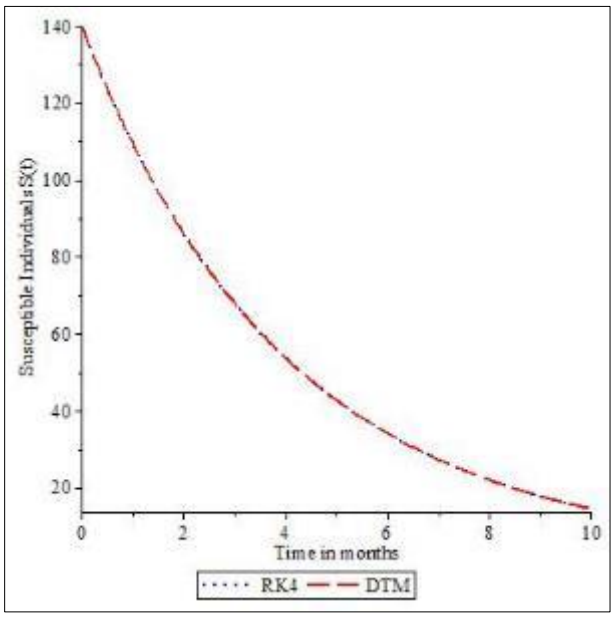

Figure 15 Comparison Plot for $\boldsymbol{S(t)}$

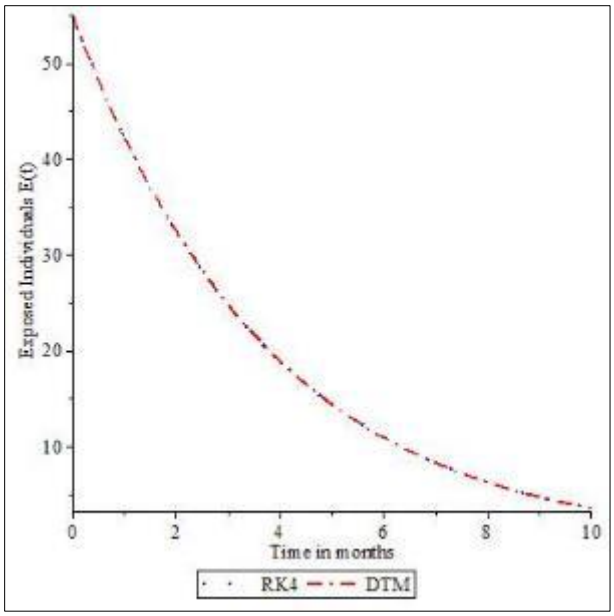

Figure 16 Comparison Plot for $\boldsymbol{E(t)}$

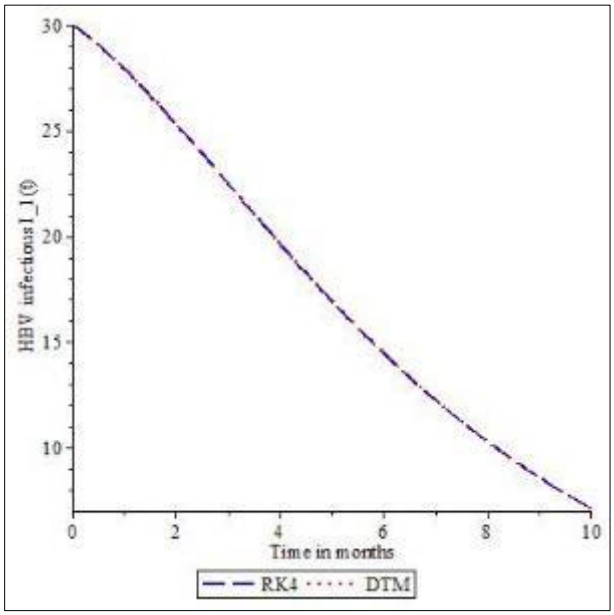

Figure 17 Comparison Plot for $\boldsymbol{I_1(t)}$

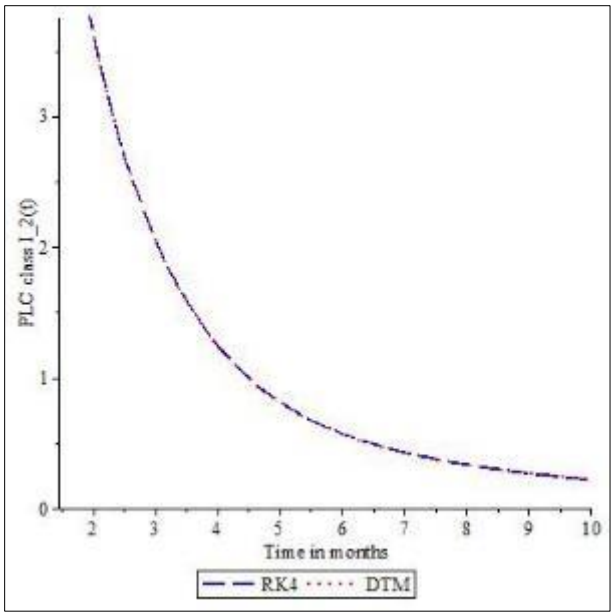

Figure 18 Comparison Plot for $\boldsymbol{I_2(t)}$

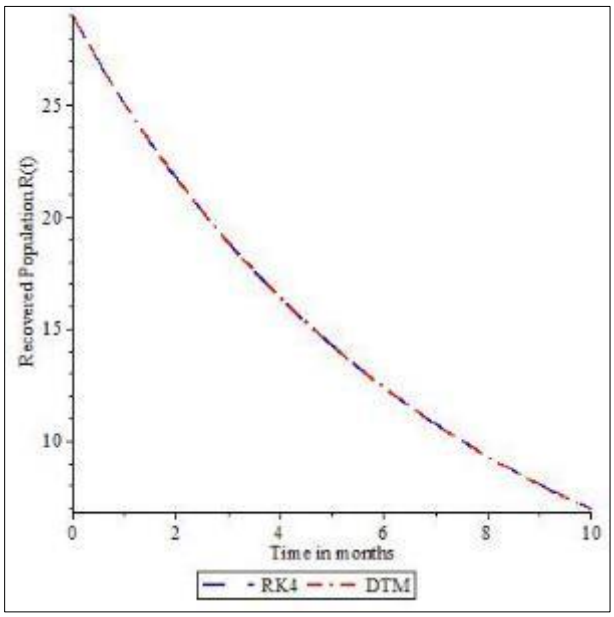

Figure 19 Comparison Plot for $\boldsymbol{R(t)}$

3. Results and discussion

A model to study the progression rate of hepatitis B virus infection (HBV) to Liver Cirrhosis (otherwise known as Primary Liver Cancer, PLC) was developed for analysis. In a bid to distort the deterioration rate of HBV to PLC, a controlled model was formulated by incoporating four distinct controls at various compartments of the model. The controlled model was analyzed based on PMP and numerically simulated to obtain figures (2) – (7). The interpretation of the plot was deductively give. We applied DTM to the developed model toobtain a semi-analytic solution. The series solution of DTM was presented in equation (16) and numerically displayed in figures (8) – (13). Furthermore, the DTM solution was numerically compared with RK4 and graphically displayed in figures (14) – (19). The comparison between the two schemes established the effectiveness of DTM to solve system of nonlinear and linear equations, as both graphs shows excellent agreement in terms of solution to the given problem. Analysis of the cntrolled model pinpoint the

importance of sensitization and vaccination (u_2, u_3) over the other two controls as both have tangible positive effect on the overall new cases of HBV and progression to PLC.

4. Conclusion

A controlled model is essential to determine the best approach to eliminate a menace or to show the best option to reduce it. In this work, a mathematical model to understand the progression rate of HBV to PLC was developed for analysis. Some fundamental qualitative analysis of the model was established, before the introduction of some controls aimed at preventing the spread of both HBV and PLC. Semi-analytic solution of the model was established by using DTM. The numerical analysis of DTM and RK4 established an excellent agreement of DTM in solving system of differential equaions; be it nonlinear or linear.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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