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A STUDY OF THE HEPATITIS B VIRUS INFECTION USING HILFER FRACTIONAL DERIVATIVE

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Abstract. Mathematical models have been used to understand the factors that control infectious disease progression in viral infections. This work considers a fractionalized model for HBV infection treating infected cells. Initially, the Hilfer fractional model has been developed for the epidemic problem. In this article analyzed the fractional form of the model for HBV infection using a numerical technique, i.e., the Laplace homotopy analysis method (LHAM). Homotopy analysis techniques, homotopy polynomials, and Laplace transforms are used to generate the suggested approach. Also, the convergence and uniqueness of the solution are considered. The obtained solutions are graphically simulated through MATLAB. The results obtained can prove helpful in the medical world. The fractional model gives important and relevant inferences to infer new information about the medical field.

1. Introduction

Hepatitis B virus is a common virus in humans that causes hepatitis. HBV causes serious health problems and is the leading cause of death globally. Hepatitis B has infected about two billion individuals, and 7,80,000 people have died as a result of it. The main cause of primary liver cancer is infectious hepatitis B infection. This illness can be spread from one person to another in a number of ways, including skin cuts or mucosa contact with an infected blood or bodily fluids, as well as semen and saliva and sharing syringes. Open sores on an infected person's body can also spread the illness from one person to the other.

The literature behind the modeling of the dynamics of hepatitis B is very rich. A number of models have been used by various authors to explain the dynamics of contagious infection like HIV, hepatitis B and vector born diseases, etc. The field of mathematical epidemiology aids in the understanding of rapid infection transmission through the use of appropriate complete models, as well as the right evaluation of control mechanism efficacy.

Mathematical modeling can be used to investigate the dynamic characteristics of HBV infection. Among the modeling attempts, a series of mathematical

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equations is critical in explaining the dynamics of the host cell, virus, and, most likely, the immune system.

HBV is the kind of Hepadnaviriade material that is turned into covalently closed circular DNA from a short (3kb) partially double-stranded circular DNA molecule (cccDNA). The nucleus of infected cells contains some copies of cccDNA and is used to produce mRNA. The full-length unspliced mRNA, pre-genome, is translated into DNA by viral polymerase for the creation of new virions [28].

HBV chiefly infects the hepatocytes entirely. The HBV can also infect the other cell types by replicating at both intra and extra hepatical cites. But infection on the cell types other than the hepatocytes is not well documented. Uninfected cells (i.e., target cells: hepocytes), infected cells, and the virus are all incorporates in the basic model. The creation of target cells occurs at a constant rate. These cells are created by differentiation of progenitor cells or by direct procreation from mature hepatocytes.

There is a lot of research on modeling the dynamics of hepatitis B: [2, 20, 22, 29, 19, 12]. Various authors have utilised a range of models to explain the dynamics of infectious infections like hepatitis B, HIV, brain tumor, and vector-borne diseases (see, e.g., [5, 10, 11, 15, 33]). Vargas–De–León [31] used a hepatocyte infection model of curable infected cells as a model for HBV infection, we have (see also [17, 23]).

The corresponding mathematical equations are

$$\left.\begin{aligned} \frac{dX}{dt} &= a - bX - cXZ + dY, \\ \frac{dY}{dt} &= cXZ - (v+d)Y, \\ \frac{dZ}{dt} &= sY - gZ, \end{aligned}\right\} \tag{1.1}$$

where

X	the density of the hepatocytes,
Y	the density of the uninfected one and the infected cells,
Z	the density of virions,
a	the production rate of the susceptible cells,
bX	the death rate,
c	the rate of infection curing,
cXZ	the infected susceptible cells,
vY	the death rate of infected hepatocytes,
sY	the rate of production of the free virions from the infected hepatocytes,
gZ	the rate of the viral particles are cleared,
d	the rate of production of uninfected hepatocytes created through curing, respectively.

The mathematical operations differentiation and integration are generalized to arbitrary (non-integer) order under the area of mathematics: fractional calculus. Recently, this area is applied at large scale in various fields [1, 32, 24, 14, 6]. Since differential equations are frequently used in science and engineering, and that's the why concept of fractional calculus (introduction of arbitrary order in them) attracted many applied researchers [7, 4, 26, 8, 16]. The fractional calculus is capable to perform integration and differentiation of fractional order [30, 9].

To understand the dynamics of biological systems using mathematical models, including the integer-order differential equations, are valuable. But, many biological systems have memory or after-effects. The models involving fractional ordered differential equations are advantageous over the integer ordered models as these classical models ignore such effects. Fractional operators are more beneficial over integer-order differential operators because of their non-local property, i.e., the system's next state is influenced by all of its prior stages as well as the current state. Due to this non-locality property of fractional operators, the nonlinear fractional model considers the full memory effects and explains the problem accurately.

Salman and Yousef [25] used a fractional model to model the phenomenon and produced a numerical solution utilising the predictor-corrector approach for numerically solving fractional differential equations.

This paper investigates the fractional form of the following HBV infection model. The use of the Hilfer fractional derivative to fractionalized the model is advantageous since it allows the use of the classical initial condition for the respective initial value problem without causing solvability issues. The non-linear model considers the entire memory effects and accurately explains the difficulty due to the non-locality of the Hilfer derivative.

The LHAM was used in the current study. This method is the outcome of modification in the homotopy analysis method with the Laplace transform technique [18]. In comparison to normal procedures, this change provides a simplified procedure for reaching the solution. In comparison with the HAM in LHAM, there is no requirement of assuming an auxiliary linear operator.

2. Mathematical preliminaries

In this section, certain definitions of fractional operators, namely, Riemann-Liouville integral and Hilfer derivative. The integral transforms required in forthcoming sections are also touched upon in this section.

Definition 2.1. Let h be a function of real value and its rth-order derivatives $(r = 1, 2, 3, ..., n)$ continuous on $(0, \infty)$. Then, the Hilfer fractional derivative of order $0 \leq \vartheta \leq 1$ and $0 \leq \mu \leq 1$ with respect to y [13] is defined as, $a \geq -\infty$

$$D_{a^+}^{\vartheta,\mu}(h(y)) = \big(I_{a^+}^{\mu(1-\vartheta)} \frac{d}{dy}(I_{a^+}^{(1-\mu)(1-\vartheta)}h)\big)(y), \tag{2.1}$$

Particular if $\mu = 0$, then $D_{a^+}^{\vartheta,0} = D_{a^+}^{\vartheta}$ R-L Derivative,
if $\mu = 1$, then ${}^{C}D_{a^+}^{\vartheta,1} = D_{a^+}^{\vartheta}$ Caputo Derivative.

Definition 2.2. Let $h : \mathbb{R}^+ \to \mathbb{R}$ be a continuous piecewise function. Then, for $y > 0$ the Riemann-Liouville fractional integral [24] of h of order $Re(\mathrm{v}) > 0$ is

$${}_0D_y^{-\mathrm{v}}h(y) = I^{\mathrm{v}}h(y) = \frac{1}{\Gamma(\mathrm{v})}\int_0^y (y-\xi)^{\mathrm{v}-1}h(\xi)d\xi. \tag{2.2}$$

Definition 2.3. Let g be a real-valued piecewise continuous function $(0, \infty)$. The Laplace transform of $g(z)$ [27] of exponential order $\alpha > 0$ with respect to

parameter z is given as follows;

$$\mathcal{L}[g(z);s] = \bar{g}(s) = \mathcal{L}[g(z)](s) = \int_0^\infty e^{-sz} g(z)dz, \quad \Re(s) > \alpha, z \geq 0. \tag{2.3}$$

Definition 2.4. For the function $\bar{g}(s)$, the inverse Laplace Transform with respect to $y \geq 0$ is given as follows [27];

$$\mathcal{L}^{-1}[\bar{g}(s);y] = g(y) = \frac{1}{2\pi i}\int_{\Gamma-i\infty}^{\Gamma+i\infty} e^{gy}\bar{g}(s)ds, \tag{2.4}$$

here $\Gamma \in \mathbb{R}$ is a constant.

Definition 2.5. The Laplace transform of the Hilfer fractional derivative is given by [13] as:

$$\mathcal{L}[D^{\mu,\mathrm{v}}h(x);p] = \frac{p\mathcal{L}[h(x)](p)}{p^{1-\mu}} - \frac{I^{(1-\mathrm{v})(1-\mu)}h(0)}{p^{(1-\mu)\mathrm{v}}} = p^\mu\mathcal{L}[h(x)](p) - \frac{I^{(1-\mathrm{v})(1-\mu)}h(0)}{p^{(1-\mu)\mathrm{v}}}. \tag{2.5}$$

3. The fractionalized HBV infection model and its solution

The fractional model is selected because of the relationship between fractional-ordered differential equations and systems with memory. This reason applies to the immune system, which develops memory B cells and T cells capable of fighting any threat due to previous experiences; these cells can also recognize and fight also capable of recognizing and fighting the same danger in the future. In integer-ordered models, on the other hand, there is no information about hepatocytes or free virions.

When system (1.1) is rearranged using definition (2.1), the following system is obtained.

$$\left.\begin{aligned} D_t^{\mu,\mathrm{v}}X(t) &= a - bX - cXZ + dY,\\ D_t^{\mu,\mathrm{v}}Y(t) &= cXZ - (\lambda+d)Y,\\ D_t^{\mu,\mathrm{v}}Z(t) &= sY - gZ. \end{aligned}\right\} \tag{3.1}$$

Let us consider

$$(1-\mu)(1-\mathrm{v}) = \theta, \quad (1-\mu)\mathrm{v} = \zeta. \tag{3.2}$$

with initial condition for the system, $X(0) = 1.73 \times 10^8$ $cell/(mL)$, $Y(0) = 0$ and $Z(0) = 400$ $copies/(mL)$.

Firstly, we taking the Laplace transform of the above system of equations and using the initial conditions

$$\left.\begin{aligned} L[X(t);k] - \frac{I^\theta X(0)}{k^{\zeta+\mu}} + \frac{1}{k^\mu}L[-a + bX + cXZ - dY] = 0,\\ L[Y(t);k] - \frac{I^\theta Y(0)}{k^{\zeta+\mu}} + \frac{1}{k^\mu}L[-cXZ + (\lambda+d)Y] = 0,\\ L[Z(t);k] - \frac{I^\theta Z(0)}{k^{\zeta+\mu}} + \frac{1}{k^\mu}L[-sY + gZ] = 0. \end{aligned}\right\} \tag{3.3}$$

Here, the non-linear operator is defined as follows:

$$N_1[\Psi_1(t,p),\Psi_2(t,p),\Psi_3(t,p)] = L[\Psi_1(t);p] - \frac{\Gamma(\theta+1)X_0}{k^{\zeta+\mu}\Gamma(2\theta+1)} + \frac{1}{k^{\mu}}L[-a+b\Psi_1+c\Psi_1\Psi_3-d\Psi_2],$$

$$N_2[\Psi_1(t,p),\Psi_2(t,p),\Psi_3(t,p)] = L[\Psi_2(t);p] - \frac{\Gamma(\theta+1)Y_0}{k^{\zeta+\mu}\Gamma(2\theta+1)} + \frac{1}{k^{\mu}}L[-c\Psi_1\Psi_3+(\lambda+d)\Psi_2],$$

$$N_3[\Psi_1(t,p),\Psi_2(t,p),\Psi_3(t,p)] = L[\Psi_3(t);p] - \frac{\Gamma(\theta+1)Z_0}{k^{\zeta+\mu}} + \frac{1}{k^{\mu}}L[-s\Psi_2+g\Psi_3],$$

where $p \in [0,1]$ is the embedding parameter and $\Psi_1(t,p)$, $\Psi_2(t,p)$ and $\Psi_3(t,p)$ are real-valued function. Now, developing the homotopy,

$$(1-p)L[\Psi_{\mathfrak{i}}(t,p) - I_{\mathfrak{i}}(t)] = h_{\mathfrak{i}}H(t)pN_{\mathfrak{i}}[\Psi_1,\Psi_2,\Psi_3], \quad \mathfrak{i}=1,2,3, \tag{3.4}$$

where $h_{\mathfrak{i}} \neq 0$ stand for auxiliary parameter, $H(t) \neq 0$ is an auxiliary function, L is the Laplace transform operator, and $I_{\mathfrak{i}}(t)$ represent the initial guess of $X(t)$, $Y(t)$ and $Z(t)$ corresponding to $\mathfrak{i}=1,2,3$. If the embedding parameter $p=0$, it gives;

$$\begin{aligned}\Psi_1(t;0) &= I_1(t),\\ \Psi_2(t;0) &= I_2(t),\\ \Psi_3(t;0) &= I_3(t),\end{aligned}$$

and for $p=1$ we get,

$$\begin{aligned}\Psi_1(t;1) &= X(t),\\ \Psi_2(t;1) &= Y(t),\\ \Psi_3(t;1) &= Z(t).\end{aligned}$$

As a result, the value of p varies from 0 to 1, the solution $\Psi_{\mathfrak{i}}(t,p)$ $(\mathfrak{i}=1,2,3)$ varies from the initial guess $I_{\mathfrak{i}}(t)$ $(\mathfrak{i}=1,2,3)$ to the solution $X(t)$, $Y(t)$ and $Z(t)$ respectively. On writing the function $\Psi_{\mathfrak{i}}(t;p)$ $(\mathfrak{i}=1,2,3)$ in the form of series using Taylor's theorem around p, we have

$$\begin{aligned}X(t;p) &= X_0(t) + \sum_{n=1}^{\infty} X_n(t)p^n,\\ Y(t;p) &= Y_0(t) + \sum_{n=1}^{\infty} Y_n(t)p^n,\\ Z(t;p) &= Z_0(t) + \sum_{n=1}^{\infty} Z_n(t)p^n,\end{aligned} \tag{3.5}$$

where

$$X_n = \frac{1}{n}\frac{\partial^n f_1(t;p)}{\partial p^n}\bigg|_{q=0},$$
$$Y_n = \frac{1}{n}\frac{\partial^n f_2(t;p)}{\partial p^n}\bigg|_{q=0},$$
$$Z_n = \frac{1}{n}\frac{\partial^n f_3(t;p)}{\partial p^n}\bigg|_{q=0}.$$

Now on making use of initial approximation $I_1(t) = X_0(t)$, $I_2 = Y_0(t)$ and $I_3(t) = Z_0(t)$, the auxiliary function $H(t) = 1$, selecting the parameter h appropriately, we reach at the result given below as the series (3.5) converges at $p = 1$.

$$X(t) = X_0(t) + \sum_{n=1}^{\infty} X_n(t),$$
$$Y(t) = X_0(t) + \sum_{n=1}^{\infty} Y_n(t),$$
$$Z(t) = X_0(t) + \sum_{n=1}^{\infty} Z_n(t).$$

Now, defining the nth-order deformation equation

$$\left.\begin{aligned} L[X_n - \phi_n X_{n-1}] &= h_1 R_{1,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)),\\ L[Y_n - \phi_n Y_{n-1}] &= h_2 R_{2,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)),\\ L[Z_n - \phi_n Z_{n-1}] &= h_3 R_{3,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)), \end{aligned}\right\} \tag{3.6}$$

where

$$\begin{aligned} R_{1,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)) &= L[X_{n-1}(t)] - (1-\phi_n)\frac{X_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)}\\ &\quad + \frac{1}{k^{\mu}} L[-a + bX_{n-1} + cA_{n-1} - dY_{n-1}], \end{aligned} \tag{3.7}$$

$$\begin{aligned} R_{2,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)) &= L[Y_{n-1}(t)] - (1-\phi_n)\frac{Y_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)}\\ &\quad + \frac{1}{k^{\mu}} L[-cA_{n-1} + (\lambda + d)Y_{n-1}], \end{aligned} \tag{3.8}$$

$$\begin{aligned} R_{3,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)) &= L[Z_{n-1}(t)] - (1-\phi_n)\frac{Z_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)}\\ &\quad + \frac{1}{k^{\mu}} L[-sY_{n-1} + gZ_{n-1}], \end{aligned} \tag{3.9}$$

respectively. On taking the inverse Laplace Transform,

$$X_n = \phi_n X_{n-1} + h_1 L^{-1} R_{1,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)),$$
$$Y_n = \phi_n Y_{n-1} + h_2 L^{-1} R_{2,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)),$$
$$Z_n = \phi_n Z_{n-1} + h_3 L^{-1} R_{3,n}(X_{n-1}(t), Y_{n-1}(t), Z_{n-1}(t)).$$

On using (3.7), (3.8), and (3.9) in above equations we obtain

$$X_n = \phi_n X_{n-1} + h_1 L^{-1}\Big[L[X_{n-1}] - (1-\phi_n)\frac{X_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)} + \frac{1}{k^\mu}L[-a + bX_{n-1} + cA_{n-1} - dY_{n-1}]\Big], \tag{3.10}$$

$$Y_n = \phi_n Y_{n-1} + h_2 L^{-1}\Big[L[Y_{n-1}] - (1-\phi_n)\frac{Y_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)} + \frac{1}{k^\mu}L[-cA_{n-1} + (\lambda+d)Y_{n-1}]\Big], \tag{3.11}$$

$$Z_n = \phi_n Z_{n-1} + h_3 L^{-1}\Big[L[Z_{n-1}] - (1-\phi_n)\frac{Z_0\Gamma(\theta+1)}{k^{\zeta+\mu}\Gamma(2\theta+1)} + \frac{1}{k^\mu}L[-sY_{n-1} + gZ_{n-1}]\Big], \tag{3.12}$$

where

$$\phi_n = \begin{cases} 0, & \text{if } n \le 1, \\ 1, & \text{if } n > 1 \end{cases}$$

A_n is the Homotopy polynomial and is expressed as

$$A_n = \frac{1}{\Gamma(n+1)}\frac{d^n}{dp^n}\left[\sum_{i=0}^{n} p^i X_i(t)\sum_{i=0}^{n} p^i Z_i(t)\right]_{p=0}. \tag{3.13}$$

For ease, we will take $H(t) = 1$, $h_1 = h_2 = h_3 = h$, and now, on use of initial approximation from the initial condition, we have $X_0 = 1.73 \times 10^8$ $cell/(mL)$, $Y_0 = 0$ and $Z_0 = 400$ $copies/(mL)$.
On using the recursive scheme (3.10), (3.11), and (3.12), we will obtain the following components of series solution,

$$X_1(t) == hX_0 - hX_0\frac{\Gamma(\theta+1)t^{\zeta+\mu-1}}{\Gamma(2\theta+1)\Gamma(\zeta+\mu)} + \frac{ht^\mu}{\Gamma(\mu+1)}(-a + bX_0 + cA_0), \tag{3.14}$$

Similarly

$$Y_1 = \frac{-c\,A_0\,h\,t^\mu}{\Gamma(\mu+1)}, \tag{3.15}$$

$$Z_1 = hZ_0 - \frac{hZ_0\Gamma(\theta+1)t^{\zeta+\mu-1}}{\Gamma(2\theta+1)\Gamma(\zeta+\mu)} + \frac{hgZ_0t^\mu}{\Gamma(\mu+1)}, \tag{3.16}$$

Now taking Laplace transform of above equations, we have

$$L[X_1(t)](k) = h\frac{X_0}{k} - \frac{hX_0\Gamma(\theta+1)}{\Gamma(2\theta+1)k^{\zeta+\mu}} + \frac{h}{k^{\mu+1}}(-a + bX_0 + cA_0),$$

$$L[Y_1(t)](k) = \frac{-chA_0}{k^{\mu+1}},$$

$$L[Z_1(t)](k) = \frac{hZ_0}{k} - \frac{hZ_0\Gamma(\theta+1)}{\Gamma(2\theta+1)k^{\zeta+\mu}} + \frac{hgZ_0}{k^{\mu+1}}.$$

Now, for $n = 2$

$$\begin{aligned} X_2(t) = (1+h)h\,X_0 + \frac{h\,t^{\mu}}{\Gamma(1+\mu)}\big[- a(h+2) + 2b\,h\,X_0 + b\,X_0 + cA_0\,h \\ + cA_0 + 2h\,c\,X_0\,Z_0\big] + \frac{t^{2\mu}h^2}{\Gamma(1+2\mu)}\big[- a\,b - a\,c\,Z_0 + b^2X_0 + c\,b\,A_0 \\ + b\,c\,X_0Z_0 + c^2A_0Z_0 - g\,c\,X_0Z_0 - c\,d\,A_0\big] - X_0\,h\,(1+h) \\ \frac{\Gamma(1+\theta)\,t^{\mu+\zeta-1}}{\Gamma(2\theta+1)\,\Gamma(\zeta+\mu)} - c\,Z_0\,X_0\,h^2\frac{\Gamma(1+\theta)\,t^{2\mu+\zeta-1}}{\Gamma(2\theta+1)\,\Gamma(\zeta+2\mu)}, \end{aligned} \tag{3.17}$$

$$\begin{aligned} Y_2 = \frac{-c\;ht^{\mu}}{\Gamma(\mu+1)}\,(2hX_0Z_0 + A_0 + hA_0) - \frac{c\;h^2t^{2\mu}}{\Gamma(2\mu+1)}\Big(hX_0Z_0 - aZ_0 + bX_0Z_0 \\ + cA_0Z_0 + A_0\lambda + A_0d\Big) + \frac{2h^2cX_0Z_0\Gamma(\theta+1)\;t^{2\mu+\zeta-1}}{\Gamma(2\theta+1)\;\Gamma(2\mu+\zeta)}, \end{aligned} \tag{3.18}$$

and

$$\begin{aligned} Z_2 = (1+h)h\,Z_0 + (1+2\,h)\frac{h\,t^{\mu}\,g\,Z_0}{\Gamma(1+\mu)} + (g^2\,Z_0 + s\,c\,A_0)\frac{t^{2\mu}\,h^2}{\Gamma(2\mu+1)} \\ - \frac{h\,Z_0\,t^{\mu+\zeta-1}}{\Gamma(2\theta+1)}\left[\frac{h+1}{\Gamma(\mu+\zeta)} + \frac{h\,t^{\mu}}{\Gamma(2\mu+\zeta)}\right]. \end{aligned} \tag{3.19}$$

Thus, we get the values of X, Y, Z as follows

$$X = X_0 + X_1 + X_2,$$

$$\begin{aligned} X(t) = (1+h)^2\,X_0 + \frac{h\,t^{\mu}}{\Gamma(\mu+1)}\big[- 3a + 2bX_0 + 2cA_0 - ah + 2bhX_0 + cA_0h \\ + 2chX_0Z_0\big] + \frac{t^{2\mu}h^2}{\Gamma(2\mu+1)}\big[- a\,b - a\,cZ_0 + b^2X_0 + b\,cA_0 + b\,cX_0Z_0 \\ + c^2A_0Z_0 - g\,cX_0Z_0 - d\,cA_0\big] - \frac{(2+h)X_0\,h\,t^{\mu+\zeta-1}\,\Gamma(\theta+1)}{\Gamma(2\theta+1)\,\Gamma(\mu+\zeta)} \\ - \frac{c\,X_0Z_0\,h^2\,t^{2\mu+\zeta-1}\,\Gamma(\theta+1)}{\Gamma(2\theta+1)\,\Gamma(2\mu+\zeta)}. \end{aligned} \tag{3.20}$$

$$Y = Y_0 + Y_1 + Y_2,$$

$$\begin{aligned} Y(t) = -\frac{c\,ht^{\mu}}{\Gamma(1+\mu)}\,(2A_0 + 2hX_0Z_0 + hA_0) + \frac{ch^2t^{2\mu}}{\Gamma(2\mu+1)}\Big[X_0Z_0g - aZ_0 + bX_0Z_0 \\ + cA_0Z_0 + A_0\lambda + A_0d\Big] + \frac{2h^2cX_0Z_0t^{2\mu+\zeta-1}\,\Gamma(\theta+1)}{\Gamma(2\theta+1)\;\Gamma(2\mu+\zeta)}, \end{aligned} \tag{3.21}$$

and

$$Z = Z_0 + Z_1 + Z_2,$$

$$Z(t) = (1+h)^2 Z_0 + \frac{2(1+h)h\,g\,Z_0 t^{\mu}}{\Gamma(1+\mu)} + \left(g^2\,Z_0 + c\,s A_0\right)\frac{h^2\,t^{2\mu}}{\Gamma(2\mu+1)} - \frac{(2+h)h\,Z_0\,t^{\mu+\zeta-1}\,\Gamma(1+\theta)}{\Gamma(2\theta+1)\;\Gamma(\mu+\zeta)} - \frac{h^2\,Z_0\,t^{2\mu+\zeta-1}\,\Gamma(1+\theta)}{\Gamma(2\theta+1)\;\Gamma(2\mu+\zeta)}. \tag{3.22}$$

4. Convergence analysis

In this section, we show that the system (3.1) has a unique solution.

Theorem 4.1. *The solution obtained for the HBV infection model* (3.1) *by the use of LHAM is unique, wherever* $0 < \omega_1, \omega_2, \omega_3 < 1$, *where* $\omega_1 = 1 + h + h\,b + h\,c\,G\,T_1$, $\omega_2 = 1 + h + hT_2(\lambda + d)$, *and* $\omega_3 = 1 + h + hgT_3$.

Proof. The solution of the fractional HBV infection model is,

$$X = \sum_{\mathfrak{q}=0}^{\infty} X_{\mathfrak{q}}(t),$$

$$Y = \sum_{\mathfrak{q}=0}^{\infty} Y_{\mathfrak{q}}(t),$$

$$Z = \sum_{\mathfrak{q}=0}^{\infty} Z_{\mathfrak{q}}(t),$$

$$X_m = (h+\phi_m)X_{m-1} + h\;L^{-1}\Big[-(1-\phi_m)\frac{X_0\;\Gamma(\theta+1)}{k^{\mu+\zeta}\;\Gamma(2\theta+1)} + \frac{1}{k^{\mu}}L\left(-a + b\;X_{m-1} + c\;A_{m-1} d\;Y_{m-1}\right)\Big],$$

$$Y_m = (h+\phi_m)Y_{m-1} + h\;L^{-1}\Big[-(1-\phi_m)\frac{Y_0\;\Gamma(\theta+1)}{k^{\mu+\zeta}\;\Gamma(2\theta+1)} + \frac{1}{k^{\mu}}L\left(-c\;A_{m-1} + (\lambda+d)\;Y_{m-1}\right)\Big],$$

$$Z_m = (h+\phi_m)Z_{m-1} + h\;L^{-1}\Big[-(1-\phi_m)\frac{Z_0\;\Gamma(\theta+1)}{k^{\mu+\zeta}\;\Gamma(2\theta+1)} + \frac{1}{k^{\mu}}L\left(-s\;Y_{m-1} + g\;Z_{m-1}\right)\Big].$$

Consider the X, Y, Z and X^{Δ}, Y^{Δ}, Z^{Δ} solution sets of the above system of equations such that $|X| \le E$, $|Y| \le F$ and $|Z| \le G$,

$$|X - X^{\Delta}| = \Big|(1+h)(X - X^{\Delta}) + hL^{-1}\Big[\frac{1}{k^{\mu}}L\big[b(X - X^{\Delta}) + cZ(X - X^{\Delta})\big]\Big]\Big|,$$

$$|Y - Y^{\Delta}| = \Big|(1+h)(Y - Y^{\Delta}) + hL^{-1}\Big[\frac{1}{k^{\mu}}L[(v+d)(Y - Y^{\Delta})]\Big]\Big|,$$

$$|Z - Z^{\Delta}| = \Big|(1+h)(Z - Z^{\Delta}) + hL^{-1}\Big[\frac{1}{k^{\mu}}L[g(Z - Z^{\Delta})]\Big]\Big|.$$

using the convolution theorem to the Laplace transform, we have

$$|X - X^{\Delta}| \leq (1+h)|X - X^{\Delta}| + h\int_0^t \left(|b(X - X^{\Delta})| + |cZ(X - X^{\Delta})|\right) \frac{(t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi,$$

$$|Y - Y^{\Delta}| \leq (1+h)|Y - Y^{\Delta}| + h\int_0^t (\lambda + d)|Y - Y^{\Delta}| \frac{(t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi,$$

$$|Z - Z^{\Delta}| \leq (1+h)|Z - Z^{\Delta}| + h\int_0^t g|Z - Z^{\Delta}| (\frac{t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi.$$

And hence

For X,

$$|X - X^{\Delta}| \leq (1+h)|X - X^{\Delta}| + h\int_0^t \left(b|X - X^{\Delta}| + cG|X - X^{\Delta}|\right) \frac{(t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi, \tag{4.1}$$

For Y,

$$|Y - Y^{\Delta}| \leq (1+h)|Y - Y^{\Delta}| + h\int_0^t (\lambda + d)|Y - Y^{\Delta}| \frac{(t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi, \tag{4.2}$$

For Z,

$$|Z - Z^{\Delta}| \leq (1+h)|Z - Z^{\Delta}| + h\int_0^t g|Z - Z^{\Delta}| (\frac{t-\xi)^{\mu}}{\Gamma(1+\mu)} d\xi. \tag{4.3}$$

Now, applying the mean value theorem

For X,

$$|X - X^{\Delta}| \leq (1+h)|X - X^{\Delta}| + h(b + c\,G)T_1\ |X - X^{\Delta}|,$$

$$or \qquad |X - X^{\Delta}| \leq (1 + h + hb + h\,c\,G)T_1\ |X - X^{\Delta}|,$$

$$or \qquad |X - X^{\Delta}| \leq |X - X^{\Delta}|\ \omega_1.$$

For Y,

$$|Y - Y^{\Delta}| \leq (1+h)|Y - Y^{\Delta}| + h(\lambda + d)T_2|Y - Y^{v}|,$$

$$or \qquad |Y - Y^{\Delta}| \leq (1 + h + h(\lambda + d)T_2)|Y - Y^{\Delta}|,$$

$$or \qquad |Y - Y^{\Delta}| \leq |Y - Y^{\Delta}|\ \omega_2.$$

For Z,

$$|Z - Z^{\Delta}| \leq (1+h)|Z - Z^{\Delta}| + hg|Z - Z^{\Delta}|T_3,$$

$$or \qquad |Z - Z^{\Delta}| \leq (1 + h + hgT_3)|Z - Z^{\Delta}|,$$

$$or \qquad |Z - Z^{\Delta}| \leq |Z - Z^{\Delta}|\ \omega_3.$$

It gives $(1-\omega_1)|X - X^{\Delta}| \leq 0$, $(1-\omega_2)|Y - Y^{\Delta}| \leq 0$ and $(1-\omega_3)|Z - Z^{\Delta}| \leq 0$. Since, $0 < \omega_1, \omega_2, \omega_3 < 1$ therefore, $|X - X^{\Delta}| = 0$, $|Y - Y^{\Delta}| = 0$ and $|Z - Z^{\Delta}| = 0$ which implies $X = X^{\Delta}$, $Y = Y^{\Delta}$ and $Z = Z^{\Delta}$. Therefore, the solution is unique. □

Theorem 4.2. *Let us suppose that B_1, B_2, and B_3 be Banach spaces and $\mathbb{G}_1$, $\mathbb{G}_2$ and $\mathbb{G}_3$ be nonlinear mapping i.e. $\mathbb{G}_1 : B_1 \longrightarrow B_1$, $\mathbb{G}_2 : B_2 \longrightarrow B_2$ and $\mathbb{G}_3 : B_3 \longrightarrow B_3$ and assume, $\|\mathbb{G}_1(X) - \mathbb{G}_1(X^{'})\| \leq \omega_1\|X - X^{'}\|$, $\forall\ X, X^{'} \in B_1$,*

$\|\mathbb{G}_2(Y)-\mathbb{G}_2(Y^{'})\| \leq \omega_2\|Y-Y^{'}\|$, $\forall\ Y, Y^{'} \in B_2$ *and* $\|\mathbb{G}_3(Z)-\mathbb{G}_3(Z^{'})\| \leq \omega_3\|Z-Z^{'}\|$, $\forall\ Z, Z^{'} \in B_3$. *Then according to Banach's fixed point theorem* [3, 21], *each mapping* $\mathbb{G}_1$, $\mathbb{G}_2$ *and* $\mathbb{G}_3$ *has a fixed point. The sequence corresponding to the solution obtained by the LHAM with* $X_0 \in \mathbb{G}_1$, $Y_0 \in \mathbb{G}_2$ *and* $Z_0 \in \mathbb{G}_3$ *chosen arbitrarily will converge to fixed point of* $\mathbb{G}_1$, $\mathbb{G}_2$ *and* $\mathbb{G}_3$ *respectively,*

$$\|X_m - X_r\| \leq \frac{\omega_1^r}{1-\omega_1}\|X_1 - X_0\| \ \ \forall\, X_m, X_r \in B_1,$$
$$\|Y_m - Y_r\| \leq \frac{\omega_2^r}{1-\omega_2}\|Y_1 - Y_0\| \ \ \forall\, Y_m, Y_r \in B_2,$$
$$\|Z_m - Z_r\| \leq \frac{\omega_3^r}{1-\omega_3}\|Z_1 - Z_0\| \ \ \forall\, Z_m, Z_r \in B_3.$$

Proof. Let us consider $(C_1[\eta_1], \|.\|)$, $(C_2[\eta_2], \|.\|)$ and $(C_3[\eta_3], \|.\|)$ of all continuous functions of η_1, η_2 and η_3 with the norm $\|g_1(t)\| = max_{t\in\eta_1}|g_1(t)|$, $\|g_2(t)\| = max_{t\in\eta_2}|g_2(t)|$ and $\|g_3(t)\| = max_{t\in\eta_3}|g_3(t)|$ respectively. Now, we will show that X_r, Y_r, and Z_r are the Cauchy sequences in the aforesaid Banach spaces.

$$\|X_m - X_r\| = max_{t\in\eta_1}\,|X_m - X_r|,$$
$$\|Y_m - Y_r\| = max_{t\in\eta_2}\,|Y_m - Y_r|,$$
$$\|Z_m - Z_r\| = max_{t\in\eta_3}\,|Z_m - Z_r|.$$

Now

$$\|X_m - X_r\| = max_{t\in\eta_1}\Big|(1+h)(X_{m-1} - X_{r-1}) + h\,L^{-1}\Big[\frac{1}{k^\mu}L\big[b(X_{m-1} - X_{r-1}) + c\,Z(X_{m-1} - X_{r-1})\big]\Big]\Big|,$$

or

$$\|X_m - X_r\| \leq max_{t\in\eta_1}\Big[(1+h)\big|X_{m-1} - X_{r-1}\big| + hL^{-1}\Big(\frac{1}{k^\mu}L\big[\big|b(X_{m-1} - X_{r-1})\big| + \big|cZ(X_{m-1} - X_{r-1})\big|\big]\Big)\Big],$$

$$\|Y_m - Y_r\| = max_{t\in\eta_2}\Big|(1+h)(Y_{m-1} - Y_{r-1}) + hL^{-1}\Big[\frac{1}{k^\mu}L\big[(\lambda+d)(Y_{m-1} - Y_{r-1})\big]\Big]\Big|,$$

or

$$\|Y_m - Y_r\| \leq max_{t\in\eta_2}\Big[(1+h)|Y_{m-1} - Y_{r-1}| + hL^{-1}\Big(\frac{1}{k^\mu}L\big[|(\lambda+d)(Y_{m-1} - Y_{r-1})|\big]\Big)\Big],$$

$$\|Z_m - Z_r\| = max_{t\in\eta_3}\Big|(1+h)(Z_{m-1} - Z_{r-1}) + hL^{-1}\Big(\frac{1}{k^\mu}L\big[g(Z_{m-1} - Z_{r-1})\big]\Big)\Big|,$$

or

$$\|Z_m - Z_r\| \leq max_{t\in\eta_3}\Big[(1+h)|Z_{m-1} - Z_{r-1}| + hL^{-1}\Big(\frac{1}{k^\mu}L\big[|g(Z_{m-1} - Z_{r-1})|\big]\Big)\Big],$$

Now applying the convolution theorem, we obtain

$$\|X_m - X_r\| \leq max_{t\in\eta_1}\Big[(1+h)|X_{m-1}-X_{r-1}| + h\int_0^t \Big(|b(X_{m-1}-X_{r-1})| + |cZ(X_{m-1}-X_{r-1})|\Big)\frac{(t-\xi)^\mu}{\Gamma(1+\mu)}d\xi\Big],$$

or

$$\|X_m - X_r\| \leq max_{t\in\eta_1}\Big[(1+h)|X_{m-1}-X_{r-1}| + h\int_0^t \Big(b|X_{m-1}-X_{r-1}| + cG|X_{m-1}-X_{r-1}|\Big)\frac{(t-\xi)^\mu}{\Gamma(1+\mu)}d\xi\Big],$$

Next, by using the integral mean value theorem, we have

$$\|X_m - X_r\| \leq max_{t\in\eta_1}\Big[(1+h)|X_{m-1}-X_{r-1}| + h\,|b(X_{m-1}-X_{r-1})| + |cZ(X_{m-1}-X_{r-1})|T_1\Big],$$

$$or \qquad \|X_m - X_r\| \leq \omega_1\|X_{m-1}-X_{r-1}\|. \tag{4.4}$$

Similarly

$$\|Y_m - Y_r\| \leq max_{t\in\eta_2}\Big[(1+h)|Y_{m-1}-Y_{r-1}| + h\big(|(\lambda+d)(Y_{m-1}-Y_{r-1})|\big)T_2\Big],$$

$$or \qquad \|Y_m - Y_r\| \leq \omega_2\|Y_{m-1}-Y_{r-1}\|, \tag{4.5}$$

and

$$\|Z_m - Z_r\| \leq max_{t\in\eta_3}\Big[(1+h)|Z_{m-1}-Z_{r-1}| + h\big(|g(Z_m-Z_r)|\big)T_3\Big],$$

$$or \qquad \|Z_m - Z_r\| \leq \omega_3\|Z_{m-1}-Z_{r-1}\|. \tag{4.6}$$

Taking $m = r+1$ gives,

$$\|X_{r+1}-X_r\| \leq \omega_1\|X_r-X_{r-1}\| \leq \omega_1^2\|X_{r-1}-X_{r-2}\| \leq ... \leq \omega_1^r\|X_1-X_0\|,$$
$$\|Y_{r+1}-Y_r\| \leq \omega_2\|Y_r-Y_{r-1}\| \leq \omega_2^2\|Y_{r-1}-Y_{r-2}\| \leq ... \leq \omega_2^r\|Y_1-Y_0\|,$$
$$\|Z_{r+1}-Z_r\| \leq \omega_3\|Z_r-Z_{r-1}\| \leq \omega_3^2\|Z_{r-1}-Z_{r-2}\| \leq ... \leq \omega_3^r\|Z_1-Z_0\|.$$

Now, on using the triangle inequality

$$\|X_m - X_r\| \leq \|X_{r+1}-X_r\| + \|X_{r+2}-X_{r+1}\| + ... + \|X_m - X_{m-1}\|.$$

Hence

$$\begin{aligned}\|X_m - X_r\| &\leq \big(\omega_1^r + \omega_1^{r+1} + ... + \omega_1^{m-1}\big)\|X_1-X_0\| \\ &\leq \omega_1^r\big(1+\omega_1+\omega_1^2+...+\omega_1^{m-r-1}\big)\|X_1-X_0\| \\ &\leq \omega_1^r\left[\frac{1-\omega_1^{m-r-1}}{1-\omega_1}\right]\|X_1-X_0\|.\end{aligned} \tag{4.7}$$

Similarly

$$\|Y_m - Y_r\| \leq \omega_2^r\left[\frac{1-\omega_2^{m-r-1}}{1-\omega_2}\right]\|Y_1-Y_0\|, \tag{4.8}$$

and

$$\|Z_m - Z_r\| \leq \omega_3^r \left[\frac{1-\omega_3^{m-r-1}}{1-\omega_3}\right] \|Z_1 - Z_0\|. \tag{4.9}$$

Since, $0 < \omega_1, \omega_2, \omega_3 < 1$, so $1-\omega_1^{m-r-1} < 1$, $1-\omega_2^{m-r-1} < 1$, and $1-\omega_3^{m-r-1} < 1$ then we obtain

$$\|X_m - X_r\| \leq \frac{\omega_1^r}{1-\omega_1} \|X_1 - X_0\|, \tag{4.10}$$

$$\|Y_m - Y_r\| \leq \frac{\omega_2^r}{1-\omega_2} \|Y_1 - Y_0\|, \tag{4.11}$$

$$\|Z_m - Z_r\| \leq \frac{\omega_3^r}{1-\omega_3} \|Z_1 - Z_0\|. \tag{4.12}$$

Since, $\|X_1 - X_0\| < \infty$, $\|Y_1 - Y_0\| < \infty$ and $\|Z_1 - Z_0\| < \infty$ so as $m \longrightarrow \infty$ then $\|X_m - X_r\| \longrightarrow 0$, $\|Y_m - Y_r\| \longrightarrow 0$ and $\|Z_m - Z_r\| \longrightarrow 0$. Hence, the sequence X_r, Y_r and Z_r each one is a Cauchy sequence in $C_1[\eta_1]$, $C_2[\eta_2]$ and $C_3[\eta_3]$ so these sequences are convergent. □

5. Discussion and results

The Hepatitis B virus is highly prevalent, and control of HB is a major public health concern worldwide. Since the assays of HBV markers were developed, the prevalence and incidence rates and the age distribution of HBV infection and HBV carriage have remained very similar across most provinces of the World for decades. This stable state, expressed as the 'equilibrium' between the virus and the human population, has provided good opportunities for using mathematical models to study the disease's dynamics.

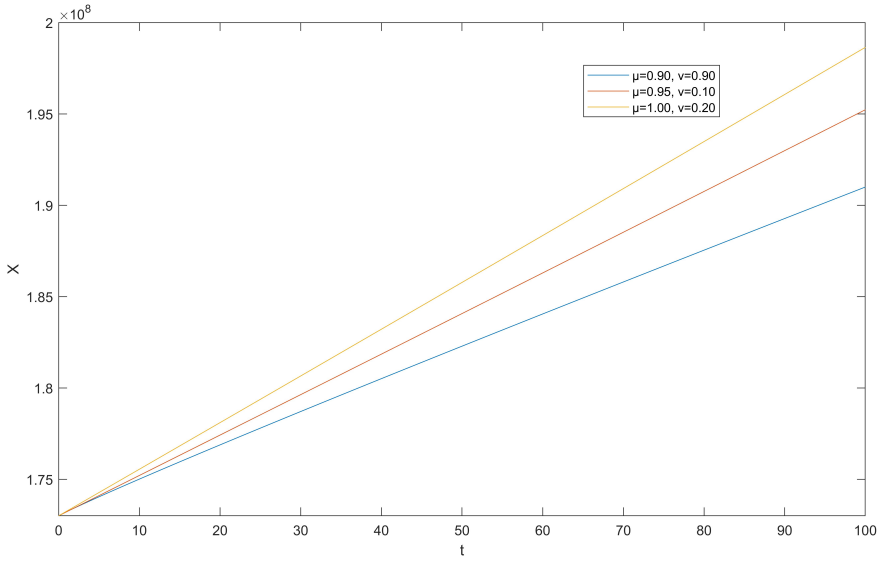

FIGURE 1. Variation of $X(t)$ for μ and v

Here we obtained a numerical simulation of the effect of fractional order derivatives on HBV. Graphs are plotted in MATLAB with the values of the parameters used here [25]: $a = 5\times10^5\ cells/(mL.\mathrm{d})$, $b = 0.003\mathrm{d}^{-1}$, $c = 4\times10^{-10}\ mL/(copies.\mathrm{d})$, $d = 0.502\mathrm{d}^{-1}$, $s = 6.24\mathrm{d}^{-1}$, $g = 0.65\mathrm{d}^{-1}$, $v = 0.1\mathrm{d}^{-1}$, $X(0) = 1.73\times10^8\ cells/(mL)$, $Y(0) = 0$, $h = 1$, and $Z(0) = 400\ copies/(mL)$. Graphs are plotted for fractional and integer order values of μ and v in the system (3.1).

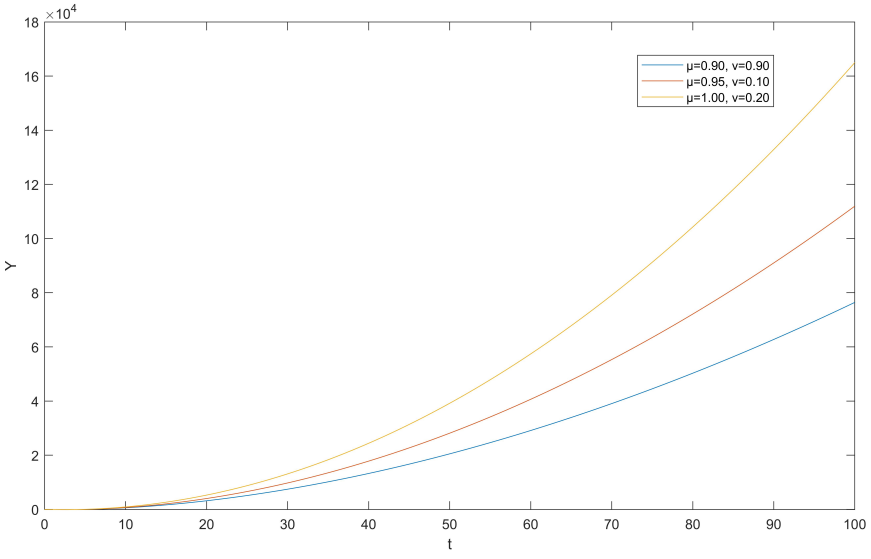

FIGURE 2. Variation of $Y(t)$ for μ and v

The dynamical behavior of the susceptible, HBV-infected, and virions is shown in the graphs. From Figure 1 for the integral value of μ, v, we observe that the susceptible cells rise with time, and the spreading of the infection is rising. But for the fractional orders, it can be revealed that the rise in susceptible units is at a slower rate as compared to the integral one, and hence, on behalf of this observation; making use of the fractional model to study the dynamics of infection the susceptible cells can be prevented from getting infected at an earlier step.

As the number of susceptible cells increases, so does the number of infected cells, as seen in Figure 2. We can see from the comparison between the integral and fractional orders in Figure 3 that the virions replicate considerably quicker for the integral values than the fractional values, resulting in disease proliferation. As a result, the fractional model is preferable to the integral model because, based on the information obtained from the fractional model study, treatment can be started at an early stage with minimal cell damage and virions replication.

6. Conclusion

This work introduces a model for HBV infection with a fractional-order derivative as a generalization of an integer-order model. The considered model is successfully examined for numerical results with the LHAM for the first few terms.

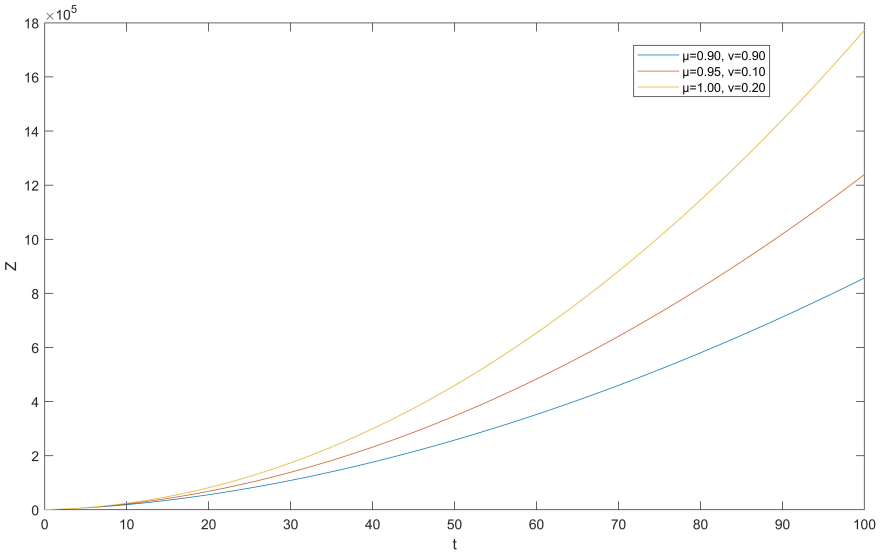

FIGURE 3. Variation of $Z(t)$ for μ and v

We have achieved numerical simulations using the LHAM method. As a whole, we can say that the fractional order differential equation comparatively achieved better prediction than that of the classical derivatives. Fractional calculus is frequently used to generalize models and aid in their more detailed elaboration. The rationale for this generalization is that, when modeling a phenomenon, some simplifications are made when considering it. In addition, it reduces the rate of variation. The fractional model is accurate and improves the results, and it has the potential to explain the computational dynamics problem in this case, which helps research hepatitis B. While this attempt to quantify the long-term benefits of targeting a high HBV prevalence population with preventive health measures has several limitations, it is consistent with the international experience of hepatitis B control. Thus, the results obtained here are general and can be very useful in applied mathematics, medical science, biochemistry, and other branches.

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