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Stability Analysis of Caputo Fractional Model for HIV Infection

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ABSTRACT

This study presents a Caputo fractional model for HIV Infection. It has been demonstrated that there is a unique non-negative and boundedness solution established in this paper. For the analysis of our Caputo fractional model for HIV infection, we proposed an in-vivo seven dimensional Caputo fractional model for the dynamics of HIV. The Caputo fractional in-vivo model is not only biologically well presented, but mathematically as well. A novel infection-free equilibrium points exists and local stability of these points are examined. Additionally, the next-generation matrix method is used to measure the basic reproductive rate of each of the HIV virus strains.

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1- Introduction

One of the major global public health issues today is the human immunodeficiency virus, commonly known as HIV. Currently, more than 35 million are infected with HIV, 71% of which live in Sub-Saharan Africa [1]. Since the onset of HIV in 1980, a lot has been accomplished in terms of its treatment [2]. The US Food and Drug Administration (FDA) approved about twenty-six HIV drugs. One of the medications used to treat HIV is known as Highly Active Antiretroviral Therapy (HAART).

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The introduction of those drugs enabled us to sustainably suppress the replication process of the virus, partially restore the defense system of the body, and sharply lower the occurrence of complications and fatality. While HAART helped us significantly in the management of HIV, the continuous use of these drugs results in different consequences and the development of a drug-resistant virus. The rise of an HIV virus that is drug resistant was also found to be caused by pre-exposure prophylaxis (PrEp), a new drug proposed to reduce the chance of infection by the non-infected person [3].

Reverse transcription is a different process that causes drug mutant HIV virus to develop. HIV is known as the RNA virus also, RNA polymers have a high rate of mutation and are not subject to verification by the host cell According to Drake and Holland [4], the mutation rate per each replication cycle for RNA viruses, such as HIV, is one mutation per genome. Therefore, all infected patients have drug-resistant mutants before they start receiving treatment, therefore, a combination therapy is needed for the HIV infection. The complexity of the resistance to HIV along with the existence of poor adherence to HIV therapy in Sub-Saharan Africa needs to be carefully analyzed. The emergence of drug resistance has been one of the most interesting problems for researchers focusing on HIV modeling aimed at the establishment of the most optimal methods of controlling the virus. The primary phenotype of the mutant strain of the HIV virus and the unmutated strain was determined through gene analysis [5], however, unfortunately, there have been no conclusive findings. Nonetheless, one finding that researchers have been able to deduce is that the infected person can pass the drug-resistant virus to another person. Researchers showed that there is a relationship between the evolution of mutated viral strains of the drug and drug adhesion [6]. The problem of the drug resistant virus has been addressed through formulated and analyzed models by mathematicians studying in-host modeling for the HIV infection. Some advantages of those models include gaining knowledge about the progression of HIV, the effectiveness of the drug, and the danger of drug-resistant viruses. For example, a five-dimensional model, which includes a wild-type and a drug-resistant strain, has been developed by Rong et al. aiming at analyzing how the lack of adherence to HAART affects drug mutant viruses [2]. Also, Reverse transcription of RNA to DNA is mutated, therefore, advising this study. This study, nevertheless, with the exception of CD8 + T-cells which are an important part the dynamics of HIV infection, There was also a six-dimensional model used by Tarfulea and Read which included two viral strains, one with sensitivity to the drug and the other without sensitivity to the drug [7]. This model did not only aim at analyzing the effectiveness of various HIV therapies also in thin each case, determining the correlation between drug effectiveness, drug resistance, and adhesion to the therapy. While this study gave helpful suggestions, also a non-infectious virus caused by the use of protease inhibitors was neglected. In a dimensional model, Tarfulea et al. he also indicated that it is important to include two strains of viruses a drug that is sensitive, as it showed the role of cells in eliminating the virus, a drug mutant and a drug-sensitive, and the role of CD8 + T-cells in the suppression of the virus. The results made it apparent that boosting the immune system should be of great importance for health care personnel working in the HIV field to reduce HIV therapy,

and therefore, lessen the issue of drug resistance. An in-vivo seven-dimensional model was developed by Ngina et al. to search for a drug that is highly effective a mong protease inhibitors, reverse transcriptase inhibitor, and protease inhibitor [8]. While this study supplied helpful findings, it neglected resistant HIV virus, which result from either long term use of HAART or previous infection with a resistant virus. Such evidence is significant in any in-vivo model.

The strategy of this paper is as follows: In section 2, we present necessary definitions of fractional derivative and fractional integral. Also, we review some important properties and theorems for stability analysis. In Section 3, the Caputo fractional model for HIV Infection is presented. In Section 4, we establish the solutions have a unique non-negative and their stability are investigated.

2- Preliminaries

In this section, we present necessary definitions of fractional derivative and fractional integral. Also, we review some important properties and theorems for stability analysis.

Definition 1 [9]. Let $f:[a,b]\to \mathbf{R}$. Then the left and right Riemann-Liouville fractional integral (RLFI) of order $\alpha>0$ of f is given by

$$ {}_aJ_t^{\alpha} f(t)=\frac{1}{\Gamma(\alpha)}\int_a^t (t-\xi)^{\alpha-1} f(\xi)d\xi \tag{1}$$

$$ {}_tJ_b^{\alpha} f(t)=\frac{1}{\Gamma(\alpha)}\int_t^b (\xi-t)^{\alpha-1} f(\xi)d\xi \tag{2}$$

Definition 2 [9]. Let $f\in C^m, a>0$ and $\alpha,a,b,t\in \mathbf{R}$. Then the left (right) Riemann-Liouville fractional derivative (RLFD) and the left (right) Caputo fractional derivative (CFD) of order $m-1<\alpha<m\in N$ of f is given by

. $$ {}_aD_t^{\alpha} f(t)=\frac{1}{\Gamma(m-\alpha)}\frac{d^m}{dt^m}\int_a^t (t-\xi)^{m-\alpha-1} f(\xi)d\xi \tag{3}$$

$$ {}_tD_b^{\alpha} f(t)=\frac{1}{\Gamma(m-\alpha)}(-1)^m\frac{d^m}{dt^m}\int_t^b (\xi-t)^{m-\alpha-1} f(\xi)d\xi \tag{4}$$

. $$ {}_a^CD_t^{\alpha} f(t)=\frac{1}{\Gamma(m-\alpha)}\int_a^t (t-\xi)^{m-\alpha-1} f^{(m)}(\xi)d\xi \tag{5}$$

$$ {}_{t}^{C}D_{b}^{\alpha} f(t) = \frac{(-1)^{m}}{\Gamma(m-\alpha)} \int_{t}^{b} (\xi - t)^{m-\alpha-1} f^{(m)}(\xi) d\xi \tag{6} $$

Property 1 [10]. Let $f_1, f_2 : [a, b] \to \mathbf{R}$. Then there are $\gamma_1, \gamma_2 \in \mathbf{R}$ such that.

$$ {}_{a}^{C}D_{t}^{\alpha}(\gamma_1 f_1(t) + \gamma_2 f_2(t)) = \gamma_1 {}_{a}^{C}D_{t}^{\alpha} f_1(t) + \gamma_2 {}_{a}^{C}D_{t}^{\alpha} f_2(t) \tag{7} $$

Property 2 [10]. Let k is constant. Then

$$ {}_{a}^{C}D_{t}^{\alpha} k = 0 \tag{8} $$

Remark 1 [11]. There is a relationship connect between RLFI and CFD as follow

$$ {}_{a}D_{t}^{\alpha} f(t) = {}_{a}^{C}D_{t}^{\alpha} f(t) + \sum_{i=0}^{m-1} \frac{f^{(i)}(a)}{\Gamma(i+1-\alpha)} (t-a)^{i-\alpha} \tag{9} $$

$$ {}_{t}D_{b}^{\alpha} f(t) = {}_{t}^{C}D_{b}^{\alpha} f(t) + \sum_{i=0}^{m-1} \frac{f^{(i)}(b)}{\Gamma(i+1-\alpha)} (t-b)^{i-\alpha} \tag{10} $$

Consider the general Caputo fractional differential equation as follow:

$$ {}_{a}^{C}D_{t}^{\alpha} x(t) = g(t, x(t)), \qquad 0 < \alpha \le 1 \tag{11} $$

Subject to

$$ x(t_0) = x_0 \tag{12} $$

Definition 3 [12]. The Caputo fractional dynamic system (11) have equilibrium point x^* if and only if $g(t, x^*) = 0$.

Theorem 1 [13]. The Caputo fractional dynamic system (11) at equilibrium point x^* is locally asymptotically stable if all the eigenvalues λ of the Jacobian matrix of system (11) at the equilibrium point x^*, satisfies the following condition:

$$ |\arg(\lambda)| > \frac{\alpha\pi}{2}. \tag{13} $$

Definition 4 [14]. Suppose that $G(s)$ is the Laplace transform of the function $G(t)$. Then, the Laplace transform of the Caputo derivative is get as follow

$$ L\{{}_{a}^{C}D_{t}^{\alpha} G(t), s\} = s^{\alpha} G(s) - \sum_{i=0}^{m-1} s^{\alpha-i-1} G^{(i)}(0), \quad m-1 < \alpha \le m, \; m \in \square \tag{14} $$

Definition 5 [14]. The generalized Mittag-Leffler function $E_{n,m}(t)$ for $t \in \square$ is defined by

$$E_{n,m}(t) = \sum_{i=0}^{\infty} \frac{t^i}{\Gamma(ni+m)} \quad , \quad n,m > 0 \tag{15}$$

Property 3 [14]. The Mittag-Leffler function $E_{n,m}(t)$ for $t \in \square$ satisfies

$$E_{n,m}(t) = t\, E_{n,n+m}(t) + \frac{1}{\Gamma(m)} \quad , \quad n,m > 0 \tag{16}$$

Definition 6 [14]. The Laplace transform of the Mittag-Leffler function $E_{n,m}(t)$ is defined as follows

$$L\{t^{m-1} E_{n,m}(\pm \beta t^n)\} = \frac{s^{n-m}}{s^n \mp} \tag{17}$$

3- Analysis of HIV Model

For the purpose of obtaining the fractional optimal control, we will subedit a mathematical sample that shows the relationship between that HIV viruses and the organ responsible for the body's immunity. In this subsection we will generalize HIV model to Caputo fractional order system of order α . The population is divided into seven sub-classes as according to the following table.

Table 1: variables for HIV in-vivo system

Variable	Description
T	The concentricity of the non-infected $CD4^+$ T-cells.
I	The concentricity of the infected $CD4^+$ T-cells.
I_l	The concentricity of latently infected $CD4^+$ T-cells.
V	The concentration of HIV virions.
V_n	The concentration of the unripe non-infectious virions.
Z	The concentricity of the $CD8^+$ T-cells..
Z_a	The concentricity of the activated $CD8^+$ T-cells.

Now, we suppose the following system of Caputo fractional equations to describe the in vivo dynamics of HIV:

$$
\begin{aligned}
&{}_0^C D_t^\alpha T = \lambda_T - \mu_T T - (1-u_1)\chi TV,\\
&{}_0^C D_t^\alpha I = (1-u_2)\chi TV - \mu_I I - \gamma I Z_a,\\
&{}_0^C D_t^\alpha I_l = u_2 \chi TV - \mu_{I_l} I_l,\\
&{}_0^C D_t^\alpha V = (1-u_3)\varepsilon_V \mu_I I - \mu_V V,\\
&{}_0^C D_t^\alpha V_n = u_3 \varepsilon_V \mu_I I - \mu_{Vn} V_n,\\
&{}_0^C D_t^\alpha Z = \lambda_z - \mu_z Z - \beta Z I,\\
&{}_0^C D_t^\alpha Z_a = \beta Z I - \mu_{Z_a} Z_a,
\end{aligned}
\tag{18}
$$

Where $0 \le u_1, u_2, u_3 \le 1$. Control u_1 represents fusion inhibitors (FIs) she knows that it is a class of antiretroviral drugs that work on the outside of the host CD4+ T-cell to prevent HIV from ,the causing human immunity to integrate with it and hence its infection also the u_2 control represents the reverse transcriptase inhibitors (RTIs) which are the reason to prevent the process of reverse transcription ,while u_3 another control that represents the Protease inhibitors (PIs) ,whose role is to prevent the secretion of the protease in the liver.

Table 2: Parameters for HIV in-vivo model

Parameter	Description
λ_T	The rate at which the non-infected $CD4^+$ T-cells are produced.
μ_T	The rate at which the non-infected $CD4^+$ T-cells dissolution.
χ	The rate at which the $CD4^+$ T-cells are infected by the virus.
μ_I	The death rate of the infected $CD4^+$ T-cells.
μ_{I_l}	The death rate of the latently infected $CD4^+$ T-cells.
ε_V	The rate in which HIV virions are produced from the infected $CD4^+$ T-cells.
μ_V	The death rate of the infectious virus.
μ_{V_n}	The death rate of the non-infectious virus.
γ	The rate at which the infected cells are eliminated by the activated $CD8^+$ T-cells.
λ_z	The rate at which the $CD8^+$ T-cells are produced.
μ_z	The death rate of the $CD8^+$ T-cells.
β	The rate at which the $CD8^+$ T-cells are activated by the presence of the virus and the infected $CD4^+$ T-cells.
μ_{Za}	The rate at which the activated defense cells decay.

4- paradigm analysis

We note that the solution to the system (18) is not negative as long as the values for its priority are not negative and the proof is our result for the first we present the following result shows the Mean value theorem.

Lemma 1 [15]. (Generalized Mean Value Theorem).

Suppose that $x(t) \in C[a,b]$ and ${}_a^C D_t^\alpha x(t) \in C(a,b]$, for $0 < \alpha \le 1$, then we have

$$x(t) = x(a) + \frac{1}{\Gamma(\alpha)} ({}_a^C D_t^\alpha x)(\xi)(t-a)^\alpha \tag{19}$$

with $\xi \in [a,t],\ \forall t \in (a,b]$.

Corollary 1 [15]. Suppose that $x(t) \in C[a,b]$ and ${}_a^C D_t^\alpha x(t) \in C(a,b]$, for $0 < \alpha \le 1$. If ${}_a^C D_t^\alpha x(t) \ge 0,\ \forall\ a < t < b$, then $x(t)$ is non-decreasing for each $a \le t \le b$. If ${}_a^C D_t^\alpha x(t) \le 0,\ \forall\ a < t < b$, then $x(t)$ is non-increasing for each $a \le t \le b$.

Theorem 2.

The territory $\Psi = \{(T, I, I_l, V, V_n, \mathrm{Z}, \mathrm{Z}_a) : T \ge 0, I \ge 0, I_l \ge 0, V \ge 0, V_n \ge 0, \mathrm{Z} \ge 0, \mathrm{Z}_a \ge 0\}$ is a positive invariant set for system (18).

Proof: From [9] the uniqueness and existence of the solution of model (18) on the time interval $(0,\infty)$ can be obtained. On the hyperplanes of territory Ψ we get

$$\begin{aligned}
&{}_0^C D_t^\alpha T\big|_{T=0} = \lambda_T > 0,\\
&{}_0^C D_t^\alpha I\big|_{I=0} = (1-u_2)\chi TV \ge 0,\\
&{}_0^C D_t^\alpha I_l\big|_{I_l=0} = u_2 \chi TV \ge 0,\\
&{}_0^C D_t^\alpha V\big|_{V=0} = (1-u_3)\varepsilon_V \mu_I I \ge 0,\\
&{}_0^C D_t^\alpha V_n\big|_{V_n=0} = u_3 \varepsilon_V \mu_I I \ge 0,\\
&{}_0^C D_t^\alpha Z\big|_{Z=0} = \lambda_Z > 0,\\
&{}_0^C D_t^\alpha Z_a\big|_{Z_a=0} = \beta ZI \ge 0,
\end{aligned} \tag{20}$$

Since $(T, I, I_l, V, V_n, \mathrm{Z}, \mathrm{Z}_a) \in \Psi$, According to the Corollary1, the solution $(T, I, I_l, V, V_n, \mathrm{Z}, \mathrm{Z}_a)$ cannot escape from the hyperplanes of $T = 0$, $I = 0, I_l = 0, V = 0$, $V_n = 0$, $\mathrm{Z} = 0, \mathrm{Z}_a = 0$; i.e. the territory Ψ is a positive invariant set.

Now, we display the boundedness of the solution of the Caputo fractional model for HIV Infection (18) by the next theorem.

Theorem 3.

The territory $\Psi = \{(T, I, I_l, V, V_n, \mathrm{Z}, \mathrm{Z}_a) : T \geq 0, I \geq 0, I_l \geq 0, V \geq 0, V_n \geq 0, \mathrm{Z} + \mathrm{Z}_a \leq \frac{\lambda_Z}{\Theta}\}$ is a positive invariant set for system (18).

Proof: From (18) the total population of the $CD8^+$ T-cells satisfy

$$ {}_0^C D_t^{\alpha} N_8(t) = \lambda_Z - \mu_z Z - \mu_{Z_a} Z_a \tag{21} $$

Where $N_8(t) = Z + Z_a$

Let $\Theta = \min\{\mu_Z, \mu_{Z_a}\}$, then from (21) we will get

$$ {}_0^C D_t^{\alpha} N_8(t) = \lambda_Z - \Theta\{Z + Z_a\} $$

$$ {}_0^C D_t^{\alpha} N_8(t) \leq \lambda_Z - \Theta N_8(t) \tag{22} $$

By applying the Laplace transform to Eq. (22), we will get

$$ s^{\alpha} \bar{N}_8(s) - s^{\alpha-1} N_8(0) \leq \frac{\lambda_Z}{s} - \Theta \bar{N}_8(s) $$

$$ (s^{\alpha} + \Theta) \bar{N}_8(s) \leq \frac{\lambda_Z}{s} + s^{\alpha-1} N_8(0) $$

$$ \bar{N}_8(s) \leq \frac{s^{-1}}{s^{\alpha} + \Theta} \lambda_Z + \frac{s^{\alpha-1}}{s^{\alpha} + \Theta} N_8(0) $$

From Eq. (17) and Eq. (16), we conclude that if $(T, I, I_l, V, V_n, \mathrm{Z}, \mathrm{Z}_a) \in \Psi$, then

$$N_8(t) \le \lambda_Z t^{\alpha} \mathrm{E}_{\alpha,\alpha+1}(-\Theta t^{\alpha}) + \mathrm{E}_{\alpha,1}(-\Theta t^{\alpha}) N_8(0)$$

$$\le \frac{\lambda_Z}{\Theta}[\Theta t^{\alpha} \mathrm{E}_{\alpha,\alpha+1}(-\Theta t^{\alpha}) + \mathrm{E}_{\alpha,1}(-\Theta t^{\alpha})]$$

$$\le \frac{\lambda_Z}{\Theta}[\Theta t^{\alpha} \mathrm{E}_{\alpha,\alpha+1}(-\Theta t^{\alpha}) - \Theta t^{\alpha} \mathrm{E}_{\alpha,\alpha+1}(-\Theta t^{\alpha}) + \frac{1}{\Gamma(1)}] = \frac{\lambda_Z}{\Theta} \tag{23}$$

Then from Theorem 2 and Eq. (23), we obtain the boundedness of $N_8(t)$ as $0 \le N_8 \le \frac{\lambda_Z}{\Theta}$. So, the feasible territory Ψ is positively invariant. This shows the solution of the Caputo fractional model for HIV Infection (18) is bounded.

4.1- Contagion-free equilibrium

The Caputo fractional model (18) has a contagion-free equilibrium which happen when I, I_l, V, V_n and Z_a are equal and given by

$$\begin{aligned} E_0 &= (T(0), I(0), I_l(0), V(0), V_n(0), Z(0), Z_a(0)) \\ &= (\frac{\lambda_T}{\mu_T}, 0, 0, 0, 0, \frac{\lambda_z}{\mu_z}, 0) \end{aligned} \tag{24}$$

4.2- The basic reproductive number

In this section, we will apply the next generation matrix in determining the identification of the marking that governs the spread of the disease, which is called the primary reproductive number [10]. Where R_0 indicates the average secondary infection cases that result from the primary condition in a group of individuals most susceptible to HIV infection in vivo. R_0 indicates the number of $CD4^+$ T-cells that result from one $CD4^+$ T-cells infected throughout their life span. The presence of R_0 <1 means that the disease can be completely eradicated and that it is done through HIV treatment that infects sensitive parameters of R_0.

4.3- Calculation of R_0

Using the next generation method R_0, where R_0 is the eigenvalue of the matrix $G = \tilde{I}\,\tilde{}$, where $\tilde{I}$ indicates new infections, while $\tilde{I}$ indicates the transmission of infection from one place

to another. Both of them are calculated in an equilibrium-free equilibrium state, and consequently is derived as follows.

From system (18) the infective compartments are

$$\begin{aligned}
&{}_0^C D_t^\alpha I = (1-u_2)\chi TV - \mu_I I - \gamma I Z_a,\\
&{}_0^C D_t^\alpha I_l = u_2 \chi TV - \mu_{I_l} I_l,\\
&{}_0^C D_t^\alpha V = (1-u_3)\varepsilon_V \mu_I I - \mu_V V,\\
&{}_0^C D_t^\alpha Z = \lambda_z - \mu_z Z - \beta Z I,\\
&{}_0^C D_t^\alpha Z_a = \beta Z I - \mu_{Z_a} Z_a,
\end{aligned} \tag{25}$$

Now we give the Matrix to transmit infection from one person to another at the point of balance free from infection.

$$\tilde{I} \begin{bmatrix}
0 & 0 & (1-u_2(\mathrm{t}))\chi \dfrac{\lambda_T}{\mu_T} & 0 & 0\\
0 & 0 & u_2 \chi \dfrac{\lambda_T}{\mu_T} & 0 & 0\\
0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0\\
\beta \dfrac{\lambda_Z}{\mu_Z} & 0 & 0 & 0 & 0
\end{bmatrix} \tag{26}$$

Now we give matrix that transfers infections from one stone to another in a balance that is free from disease.

$$\tilde{I} \begin{bmatrix}
\mu_I & 0 & 0 & 0 & 0\\
0 & \mu_{I_l} & 0 & 0 & 0\\
(1-u_3)\varepsilon_V \mu_I & 0 & \mu_V & 0 & 0\\
\beta \dfrac{\lambda_Z}{\mu_Z} & 0 & 0 & \mu_Z & 0\\
0 & 0 & 0 & 0 & \mu_{Z_a}
\end{bmatrix} \tag{27}$$

The inverse of matrix $\tilde{I}$ from is given by

$$\tilde{I} \begin{bmatrix} \frac{1}{\mu_I} & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{\mu_{I_l}} & 0 & 0 & 0 \\ (1-u_3)\varepsilon_V & 0 & \frac{1}{\mu_V} & 0 & 0 \\ \mu_V & & & & \\ -\beta\frac{\lambda_Z}{\mu_Z^2\mu_I} & 0 & 0 & \frac{1}{\mu_Z} & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\mu_{Z_a}} \end{bmatrix} \tag{28}$$

By multiplying matrices (26) and (28) we will get

$$\tilde{I}\tilde{} \begin{bmatrix} \frac{(1-u_2)(1-u_3)\chi\lambda_T\varepsilon_V}{\mu_T\mu_V} & 0 & \frac{(1-u_2)\chi\lambda_T}{\mu_T\mu_V} & 0 & 0 \\ \frac{u_2\chi\lambda_T(1-u_3)\varepsilon_V}{\mu_T\mu_V} & 0 & \frac{u_2\chi\lambda_T}{\mu_T\mu_V} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ \beta\frac{\lambda_Z}{\mu_Z\mu_I} & 0 & 0 & 0 & 0 \end{bmatrix} \tag{29}$$

The eigenvalues from the matrix (29) are

$$\lambda = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ (u_3-1)(u_2-1)\frac{\chi\varepsilon_V\lambda_T}{\mu_T\mu_V} \end{bmatrix} \tag{30}$$

It is from eigenvalues the reproductive number is essentially known as

$$R_0 = (u_3-1)(u_2-1)\frac{\chi\varepsilon_V\lambda_T}{\mu_T\mu_V} \tag{31}$$

We note that if the $R_0 < 1$ is viral, the human immunodeficiency virus (HIV) will note be able to control the disease will and with time. Time is a very important factor because the virus is undetectable which depends on the small size of R_0, and therefore it is necessary to continue in taking HARRT in order to avoid illness .

4.4- Analysis of the R_0

In this section ,we aim to determine the relative importance of the various parameters that are responsible for viral reproduction ,which is related to R_0, and which is a measure of the possibility of infection spreading between people and is considered one of the most important ideas that present by mathematicians to the epidemiology to date [16], there are several methods for conducting an allergy analysis ,all aiming to classify a sensitivity that is slightly different in this study.

The normalized forward sensibility index of R_0 with respect to the parameter Q is given by:

$$\gamma_Q^{R_0} = \left(\frac{\partial R_0}{\partial Q}\right)\left(\frac{Q}{R_0}\right) \tag{32}$$

Where Q indicates the basic reproductive number from which is given by Eq. (31) and that the sensitivity indicators R with respect to the parameters $\chi, \varepsilon_V, \lambda_T, \mu_T, \mu_V$ are, respectively, given as:

$$\frac{\partial R_0}{\partial \chi}\frac{\chi}{R_0} = (u_3-1)(u_2-1)\frac{\varepsilon_V \lambda_T}{\mu_T \mu_V}\frac{\chi}{(u_3-1)(u_2-1)\frac{\chi \varepsilon_V \lambda_T}{\mu_T \mu_V}} = 1 \tag{33}$$

$$\frac{\partial R_0}{\partial \varepsilon_V}\frac{\varepsilon_V}{R_0} = (u_3-1)(u_2-1)\frac{\chi \lambda_T}{\mu_T \mu_V}\frac{\varepsilon_V}{(u_3-1)(u_2-1)\frac{\chi \varepsilon_V \lambda_T}{\mu_T \mu_V}} = 1 \tag{34}$$

$$\frac{\partial R_0}{\partial \lambda_T}\frac{\lambda_T}{R_0} = (u_3-1)(u_2-1)\frac{\chi \varepsilon_V}{\mu_T \mu_V}\frac{\lambda_T}{(u_3-1)(u_2-1)\frac{\chi \varepsilon_V \lambda_T}{\mu_T \mu_V}} = 1 \tag{35}$$

$$\frac{\partial R_0}{\partial \mu_T}\frac{\mu_T}{R_0} = -(u_3-1)(u_2-1)\frac{\chi \varepsilon_V}{\mu_T^2 \mu_V}\frac{\mu_T}{(u_3-1)(u_2-1)\frac{\chi \varepsilon_V \lambda_T}{\mu_T \mu_V}} = -1 \tag{36}$$

$$\frac{\partial R_0}{\partial \mu_V}\frac{\mu_V}{R_0} = -(u_3-1)(u_2-1)\frac{\chi\varepsilon_V}{\mu_T\mu_V^2}\frac{\mu_V}{(u_3-1)(u_2-1)\frac{\chi\varepsilon_V\lambda_T}{\mu_T\mu_V}} = -1 \tag{37}$$

We note that through sensitivity indicators ,it becomes clear to us that χ, ε_V and λ_T are among the most positively sensibility parameters ,and this will lead to an increase in the value of R .at the same time that μ_T and μ_V is one of the sensitivity parameters negative and therefore increasing any of these parameters will reduce the value of R and in particular that an increase of 1 in R and the results that in turn led to a decrease of 1 in R, and therefore physicians who are healthy should use the controls that affect allergic parameters for the most positive and therefore will lead to a decrease in the number of HIV viruses

Also, note of the R_0 (30) is that if $u_2 = u_3 = 1$ then the basic reproductive number equal to zero with this result the disease will be completely eradicated

4.5- Local stability of the contagion-free balance

Theorem 4. The infection-free balance, E_0, is locally asymptotically stable when $R_0 < 1$ and unstable otherwise.

Proof: To determine local stability and equilibrium without infection, we apply a linear method and thus give the Jacobian matrix of Caputo fractional system as follows:

$$\tilde{\cdot} \begin{bmatrix} -\mu_T & 0 & 0 & -(1-u_1)\chi\frac{\lambda_T}{\mu_T} & 0 & 0 & 0 \\ 0 & -\mu_I & 0 & (1-u_2)\chi\frac{\lambda_T}{\mu_T} & 0 & 0 & 0 \\ 0 & 0 & -\mu_{I_L} & u_2\chi\frac{\lambda_T}{\mu_T} & 0 & 0 & 0 \\ 0 & (1-u_3)\varepsilon_V\mu_I & 0 & -\mu_V & 0 & 0 & 0 \\ 0 & u_3\varepsilon_V\mu_I & 0 & 0 & -\mu_{V_n} & 0 & 0 \\ 0 & -\beta\frac{\lambda_Z}{\mu_Z} & 0 & 0 & 0 & -\mu_Z & 0 \\ 0 & \beta\frac{\lambda_Z}{\mu_Z} & 0 & 0 & 0 & 0 & -\mu_{Z_a} \end{bmatrix} \tag{38}$$

Now, we extract the eigenvalues of the Jacobian matrix in Eq. (38) as follow

$$\lambda_1 = -\mu_{Z_a} \tag{39}$$

$$\lambda_2 = -\mu_Z \tag{40}$$

$$\lambda_3 = -\mu_{Vn} \tag{41}$$

$$\lambda_4 = -\mu_T \tag{42}$$

$$\lambda_5 = -\mu_{I_l} \tag{43}$$

$$\lambda_6 = \frac{-(\mu_T\mu_I + \mu_T\mu_V) + \sqrt{4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2}}{2\mu_T} \tag{44}$$

$$\lambda_7 = \frac{-(\mu_T\mu_I + \mu_T\mu_V) + \sqrt{4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2}}{2\mu_T} \tag{45}$$

Note that $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ and λ_5 have a real negative part. Now, we will proof the λ_6 and λ_7 have a real negative part.

Since $\lambda_6 = \lambda_7$, then suppose $\lambda_6 < 0$, we get

$$\frac{-(\mu_T\mu_I + \mu_T\mu_V) + \sqrt{4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2}}{2\mu_T} < 0$$

$$-(\mu_T\mu_I + \mu_T\mu_V) + \sqrt{4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2} < 0$$

$$\sqrt{4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2} < (\mu_T\mu_I + \mu_T\mu_V)$$

$$4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + (\mu_T\mu_I - \mu_T\mu_V)^2 < (\mu_T\mu_I + \mu_T\mu_V)^2$$

$$4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi + \mu_T^2\mu_I^2 - 2\mu_T^2\mu_I\mu_V + \mu_T^2\mu_V^2 < \mu_T^2\mu_I^2 + 2\mu_T^2\mu_I\mu_V + \mu_T^2\mu_V^2$$

$$4(1-u_2)(1-u_3)\lambda_T\mu_T\mu_I\varepsilon_V\chi - 4\mu_T^2\mu_I\mu_V < 0$$

$$(1-u_2)(1-u_3)\frac{\lambda_T \varepsilon_V \chi}{\mu_T \mu_V} < 1$$

$$(u_2-1)(u_3-1)\frac{\lambda_T \varepsilon_V \chi}{\mu_T \mu_V} < 1 \qquad (46)$$

Since $R_0 = (u_2-1)(u_3-1)\frac{\lambda_T \varepsilon_V \chi}{\mu_T \mu_V}$, then from (46) we have $R_0 < 1$. Then infection-free balance, E_0, is locally asymptotically stable.

5- Conclusion

This study formulated and analyzed a Caputo fractional model for HIV infection. The qualitative analysis of the model shows that the solutions of the model are bounded and positive. The infection-free equilibrium point of the model is obtained and its local condition investigated in reference to the basic reproduction number, in which the results indicate that the infection-free equilibrium of the model is both locally stable.

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