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Research Article

A Fractional-Order Model for HIV Dynamics in a Two-Sex Population

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Human Immunodeficiency Virus (HIV) is a virus that attacks or infects cells in the immune system that causes immune decline. Acquired Immunodeficiency Syndrome (AIDS) is the most severe stage of HIV infection. AIDS is the rapidly spreading and becoming epidemic diseases in the world of almost complete influence across the country. A mathematical model approach of HIV/AIDS dynamic is needed to predict the spread of the diseases in the future. In this paper, we presented a fractional-order model of the spread of HIV and AIDS diseases, which incorporates two-sex population. The fractional derivative order of the model is in the interval $(0, 1]$. We compute the basic reproduction number and prove the stability of the equilibriums of the model. The sensitivity analysis also is done to determine the important factor controlling the spread. Using the Adams-type predictor-corrector method, we then perform some numerical simulations for variation values of the order of the fractional derivative. Finally, the effects of various antiretroviral therapy (ART) treatments are studied and compared with numerical approach.

1. Introduction

Human Immunodeficiency Virus (HIV) is a virus that attacks or infects cells in the immune system that causes immune decline. Acquired Immunodeficiency Syndrome (AIDS) is the most severe stage of HIV infection, which can take from 2 to 15 years to develop depending on the individual. AIDS is defined by the development of certain cancers, infections, or other severe clinical manifestations. HIV can be transmitted via the exchange of a variety of body fluids from infected individuals, such as blood, breast milk, semen, and vaginal secretions. There were approximately 36.7 million people living with HIV at the end of 2016 with 1.0 million people died from HIV-related causes globally. In 2015, an estimated 44% of new infections occurred among key populations and their partners [1].

Until now, there is no cure for HIV infection. However, effective antiretroviral therapy (ART) can inhibit HIV progression in immune defects. Since 1996, ART has begun to be used by people living with HIV in the world because it can prevent death early [2]. The benefits of ART for

people with HIV/AIDS are to improve quality of life, prevent mother-to-child transmission of HIV, prolong survival, and restore the immune system [3]. In 2016, 19.5 million people with HIV have been receiving ART globally [1].

Mathematical models are needed to understand the dynamics of epidemic infection [4–8]. At present many models have been proposed to describe the dynamics of HIV/AIDS infection [9–11]. For instance, authors in [9] formulated a mathematical model for the transmission dynamics of HIV/AIDS in a two-sex population considering counseling and antiretroviral therapy. Authors in [10] studied the impact of the optimal control on the treatment of HIV/AIDS incorporating use of condom, screening of unaware infective, and treatment of HIV individuals. In recent year, Yang et al. [11] formulated a two-group (female sex workers and senior male clients) compartmental model to study the impact of senior male clients on the transmission dynamics, the containment, and the elimination of the HIV.

Memory effect plays an important role in the spread of disease. The presence of memory effects on past events

will affect the spread of disease in the future so that the spread of disease in the future can be controlled. The distance of memory effect indicates the history of disease spread. Thus, memory effects on the spread of infectious diseases can be investigated using fractional derivatives. Fractional derivatives have been used in the literature to observe the effect of memory on a system dynamics by replacing the ordinary derivative order with the fractional derivative order [12–15]. Sardar et al. [13] formulated the dengue model with memory in the transmission process by using fractional differential operator and order of the fractional derivative as an index of memory. Huo et al. [12] analyzed the effects of vaccines on mathematical models of fractional order of HIV disease spread. They also performed a local stability analysis on the fractional-order framework of HIV disease spread and bifurcation behavior of the system. In 2017, Saeedian et al. [14] studied the evolution of the SIR epidemic model, considering memory effects. Using the fractional calculus technique, the authors in [14] show that the dynamics of such a system depend on the strength of memory effects, controlled by the order of fractional derivatives. In 2017, Pinto and Carvalho [15] derived a fractional-order model for the dynamics of the coinfection of HIV and TB in the presence of TB resistant strains.

In this paper, we proposed a fractional order of two-sex mathematical model for dynamic HIV transmission, as a generalization of an integer model, proposed by Kimbir et al. [9]. We also modified the basic model in [9] by distinguishing populations infected with HIV and infected with AIDS. By using fractional ordinary differential equation, we hope that the fractional-order model can accommodate the real phenomenon of the spread of HIV/AIDS. The structure of the paper is organized as follows. In Section 2, we introduce the description of the fractional order of the HIV/AIDS model. In Section 3, the stability analysis of the equilibriums of the model is proven. In Section 4, we carry out the sensitivity analysis of the reproduction number to the parameters in the model. Section 5 shows some numerical results for distinct values of the fractional order α . Finally, in Section 6, we give a brief conclusion.

2. Description of the Model

In this section we propose a mathematical model of two-sex HIV/AIDS transmission based on [9]. The model is constructed under the following assumptions:

- (1) The total population is divided into two groups, namely, the population of males and females.
- (2) The population of males is divided into three compartments: the susceptible males (S_m), the HIV infected males (I_m), and the AIDS infected males (A_m). The population of females is also divided into three compartments: the susceptible females (S_f), the HIV infected females (I_f), and the AIDS infected females (A_f). Moreover, the total population of males

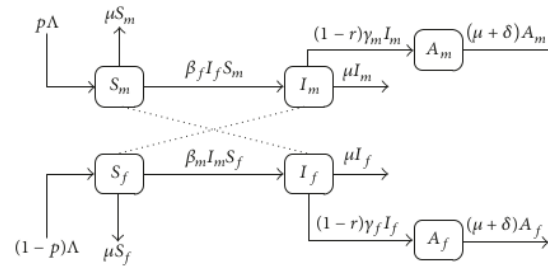


FIGURE 1: HIV/AIDS transmission diagram.

and females is given by $N = S_m + I_m + A_m + S_f + I_f + A_f$.

- (3) The HIV transmission is by heterosexual contact only.
- (4) Vertical transmission and age-structure are ignored.
- (5) The population is homogeneous mixing.
- (6) Male and female AIDS populations were isolated and then do not contribute to HIV infection.

The transmission diagram of the model is shown in Figure 1. The basic model is derived as follows:

$$\begin{aligned}
 \frac{dS_m}{dt} &= p\Lambda - \beta_f I_f S_m - \mu S_m, \\
 \frac{dI_m}{dt} &= \beta_f I_f S_m - (1-r)\gamma_m I_m - \mu I_m, \\
 \frac{dA_m}{dt} &= (1-r)\gamma_m I_m - (\mu + \delta) A_m, \\
 \frac{dS_f}{dt} &= (1-p)\Lambda - \beta_m I_m S_f - \mu S_f, \\
 \frac{dI_f}{dt} &= \beta_m I_m S_f - (1-r)\gamma_f I_f - \mu I_f, \\
 \frac{dA_f}{dt} &= (1-r)\gamma_f I_f - (\mu + \delta) A_f,
 \end{aligned} \tag{1}$$

The description of the parameter for model (1) could be seen in Table 1. The biologically feasible region of model (1) is

$$\Omega = \left\{ (S_m, I_m, A_m, S_f, I_f, A_f) \in \mathbb{R}_+^6 : 0 \leq N \leq \frac{\Lambda}{\mu} \right\}, \tag{2}$$

and all of the parameters used in model (1) are nonnegative.

The region Ω is positively invariant. In this region, model (1) is well-posed. So, if it is given an initial condition in the region, then the solution is defined for all time $t \geq 0$ and remains in the region.

Next, we consider a fractional-order model of system (1). The fractional model corresponding to system (1) is as follows:

$$\begin{aligned}
 \frac{d^\alpha S_m}{dt^\alpha} &= p\Lambda - \beta_f I_f S_m - \mu S_m, \\
 \frac{d^\alpha I_m}{dt^\alpha} &= \beta_f I_f S_m - (1-r)\gamma_m I_m - \mu I_m, \\
 \frac{d^\alpha A_m}{dt^\alpha} &= (1-r)\gamma_m I_m - (\mu + \delta) A_m, \\
 \frac{d^\alpha S_f}{dt^\alpha} &= (1-p)\Lambda - \beta_m I_m S_f - \mu S_f, \\
 \frac{d^\alpha I_f}{dt^\alpha} &= \beta_m I_m S_f - (1-r)\gamma_f I_f - \mu I_f, \\
 \frac{d^\alpha A_f}{dt^\alpha} &= (1-r)\gamma_f I_f - (\mu + \delta) A_f,
 \end{aligned}
 \tag{3}$$

where $\alpha \in (0, 1]$ is the order of the fractional derivative. Fractional derivative of model (3) is in the sense of Caputo. The Caputo approach is mostly used in real applications. The main advantages of Caputo approach are the initial values for fractional differential equations with the Caputo derivatives taking on the same form as for integer order differential equations [16]. The Caputo fractional derivative is defined as follows.

Definition 1 (see [16]). The Caputo fractional differential operator of order $\alpha > 0$, with $n - 1 < \alpha < n$, $n \in \mathbb{N}$, is defined by

$$\begin{aligned}
 \frac{d^\alpha f(t)}{dt^\alpha} &:= I^{n-\alpha} \frac{d^n f(t)}{dt^n} \\
 &= \frac{1}{\Gamma(n-\alpha)} \int_0^t (t-s)^{(n-\alpha-1)} f^{(n)}(s) ds,
 \end{aligned}
 \tag{4}$$

where $\Gamma(\cdot)$ is the gamma function.

3. Model Analysis

In this section, we study the stability of the equilibrium of the fractional-order model (3). We begin by computing the basic reproduction number (R_0) of model (3). The basic reproduction number is defined as the number of secondary cases of primary case during the infectious period due to the type of infection [17, 18].

Now, we recall the properties of the stability of the fractional-order systems. The stability theorem on fractional-order system is as follows.

TABLE 1: Parameters of model (1).

Description	Parameter
Recruitment rate	Λ
Proportion of the recruitment rate	p
Natural death rate	μ
Transmission rate by an infected male	β_m
Transmission rate by an infected female	β_f
Progression rate from male HIV infection to AIDS	γ_m
Progression rate from female HIV infection to AIDS	γ_f
AIDS disease induced death rate	δ
Proportion of the efficacy of ART treatment for HIV infection	r

Theorem 2 (see [19, 20]). Consider the following autonomous nonlinear fractional-order system:

$$\begin{aligned}
 \frac{d^\alpha x}{dt^\alpha} &= f(x), \\
 x(0) &= x_0,
 \end{aligned}
 \tag{5}$$

with $0 < \alpha < 1$ and $x \in \mathbb{R}^n$. The equilibrium points of the above system are solutions to the equation $f(x) = 0$. An equilibrium is locally asymptotically stable if all eigenvalues (λ_j) of the Jacobian matrix $J = \partial f / \partial x$ evaluated at the equilibrium satisfy $|\arg(\lambda_j)| > \alpha\pi/2$.

Based on Theorem 2, the equilibria are obtained by setting the right-hand sides of the equations in model (3) to zero. The disease-free equilibrium of model (3) to the coordinate $(S_m, I_m, A_m, S_f, I_f, A_f)$ is given by $E_0 = (\Lambda p / \mu, 0, 0, \Lambda(1-p) / \mu, 0, 0)$.

Then, the basic reproduction number (R_0) is computed by using the next-generation method [21, 22]. For the next-generation matrix method [22], we take the infected compartments (I_m, I_f). The Jacobian matrices F and V for the new infection in the compartment and the transfer of individuals between the compartment respectively, evaluated at E_0 , are given by

$$\begin{aligned}
 F &= \begin{pmatrix} 0 & \beta_f \Lambda p \\ \beta_m \Lambda (1-p) & \mu \end{pmatrix}, \\
 V &= \begin{pmatrix} 1 & 0 \\ (1-r)\gamma_m + \mu & 1 \\ 0 & (1-r)\gamma_f + \mu \end{pmatrix}.
 \end{aligned}
 \tag{6}$$

⁶⁵ The basic reproduction number of model (3) ¹⁵ is the spectral radius of the matrix FV^{-1} such that we have

$$R_0 = \frac{\Lambda}{\mu} \sqrt{\frac{\beta_m \beta_f p (1-p)}{((1-r)\gamma_m + \mu)((1-r)\gamma_f + \mu)}}. \quad (7)$$

The following theorem provides the local stability of the disease-free equilibrium. ¹⁸

Theorem 3. The disease-free equilibrium E_0 is locally asymptotically stable if $R_0 < 1$.

Proof. The Jacobian matrix of model (3) around the disease-free equilibrium, E_0 , is given by ²⁷

$$J = \begin{pmatrix} -\mu & 0 & 0 & 0 & \frac{-\beta_f p \Lambda}{\mu} & 0 \\ 0 & -(1-r)\gamma_m - \mu & 0 & 0 & \frac{\beta_f p \Lambda}{\mu} & 0 \\ 0 & (1-r)\gamma_m & -\mu - \delta & 0 & 0 & 0 \\ 0 & \frac{\beta_m \Lambda (p-1)}{\mu} & 0 & -\mu & 0 & 0 \\ 0 & -\frac{\beta_m \Lambda (p-1)}{\mu} & 0 & 0 & -(1-r)\gamma_f - \mu & 0 \\ 0 & 0 & 0 & 0 & (1-r)\gamma_f & -\mu - \delta \end{pmatrix}. \quad (8)$$

The eigenvalues of matrix J are $\lambda_1 = \lambda_2 = -\mu$ and $\lambda_3 = \lambda_4 = -(\mu + \delta)$ and the roots of quadratic equation $x^2 + a_1 x + a_2 = 0$, where $a_1 = 2(1-r)\mu(\gamma_m + \gamma_f)$ and $a_2 = [(1-r)^2 \gamma_m \gamma_f + \mu(1-r)(\gamma_m + \gamma_f) + \mu^2](1-T_0)$, with $R_0 = \sqrt{T_0}$. Thus, we have $|\arg(\lambda_1)| = |\arg(\lambda_2)| = |\arg(\lambda_3)| = |\arg(\lambda_4)| = \pi > \alpha\pi/2$. Next, we check the roots of the quadratic equation $x^2 + a_1 x + a_2 = 0$. Authors in [23] show that the Routh-Hurwitz criteria, $a_1, a_2 > 0$, are necessary and sufficient for $|\arg(\lambda_j)| > \alpha\pi/2$. It is clear that all of the eigenvalues are negative ($|\arg(\lambda_j)| > \alpha\pi/2$, for $j = 1, 2, \dots, 6$) if $T_0 < 1$ or equivalently $R_0 < 1$. Hence, the disease-free equilibrium E_0 is locally asymptotically stable for $\alpha \in (0, 1]$ if $R_0 < 1$. \square

We continue with the computing of the endemic equilibrium (E_1) of model (3). The endemic equilibrium E_1 is given by

$$E_1 = (S_m^*, I_m^*, A_m^*, S_f^*, I_f^*, A_f^*), \quad (9)$$

where

$$\begin{aligned} S_m^* &= \frac{p\Lambda}{\beta_f I_f^* + \mu}, \\ I_m^* &= \frac{(1-r)\gamma_m + \mu [(1-r)\gamma_f + \mu] \mu^2 [T_0 - 1]}{\beta_m [(1-r)\gamma_m + \mu] [\beta_f \Lambda (1-p) + ((1-r)\gamma_f + \mu) \mu]}, \end{aligned}$$

$$A_m^* = \frac{(1-r)\gamma_m I_m^*}{\mu + \delta},$$

$$S_f^* = \frac{(1-p)\Lambda}{\beta_m I_m^* + \mu},$$

$$I_f^* = \frac{\beta_m I_m^* (1-p)\Lambda}{[(1-r)\gamma_f + \mu] [\beta_m I_m^* + \mu]},$$

$$A_f^* = \frac{(1-r)\gamma_f I_f^*}{\mu + \delta}, \quad (10)$$

with $R_0 = \sqrt{T_0}$. The endemic equilibrium E_1 exists if $T_0 > 1$ or equivalently $R_0 > 1$.

The stability of the endemic equilibrium E_1 is difficult to prove analytically, because it involves a quartic equation which depend on the variables I_m and I_f . Numerical simulations show that the endemic equilibrium is locally asymptotically stable if $R_0 > 1$. This can be seen in Figures 2 and 3. Using three different initial conditions for the simulation, these orbits converge to the same point as time evolves.

4. Sensitivity Analysis ⁴²

In this section we present the sensitivity analysis of the reproduction number R_0 to the parameters in model (3). The aim of this analysis was to measure the parameters that have the most effects on the reproduction number. We derived

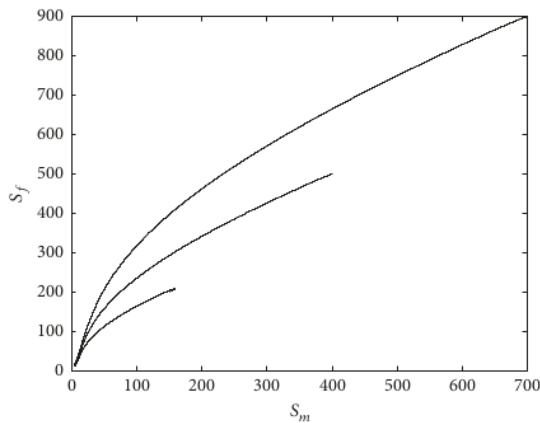


FIGURE 2: Phase portrait of model (3) in S_m - S_f plane for $\alpha = 0.8$.

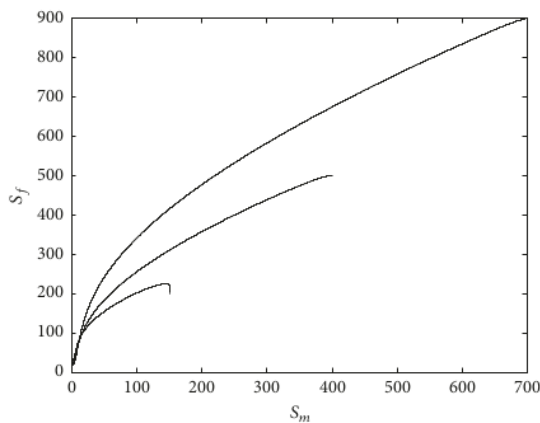


FIGURE 3: Phase portrait of model (3) in S_m - S_f plane for $\alpha = 0.9$.

analytically the sensitivity index of R_0 to each parameter following the approach in [24].

Definition 4 (see [24]). The normalized forward sensitivity index of a variable, R_0 , that depends differentially on a parameter, l , is defined as

$$Y_l^{R_0} := \frac{\partial R_0}{\partial l} \times \frac{l}{R_0}. \tag{11}$$

Based on Definition 4, the sensitivity indices of R_0 with respect to each parameter such as $\Lambda, \mu, \beta_m, \beta_f, \gamma_m, \gamma_f$, and p can be computed in the same way as (11). For example, the sensitivity index of R_0 with respect to Λ is

$$Y_\Lambda^{R_0} := \frac{\partial R_0}{\partial \Lambda} \times \frac{\Lambda}{R_0} = 1. \tag{12}$$

4.4

TABLE 2: Parameter values for simulations.

Parameter	Value	Ref.
p	0.5	Assumed
Λ	20	[12]
β_m	2×10^{-3}	Assumed
β_f	5×10^{-3}	Assumed
μ	0.02	[12]
δ	0.125	[12]
γ_m	8×10^{-3}	Assumed
γ_f	9×10^{-3}	Assumed
r	0.5	Assumed

TABLE 3: Sensitivity indices to parameter for model (3).

Parameter	Sensitivity index
Λ	1
β_m	0.5
β_f	0.5
r	0.175
μ	-1.825
γ_f	-0.092
γ_m	-0.083
p	0

Thus, we compute the sensitivity indexes of the remaining parameters using the parameter values in the Table 2. The results are given in Table 3.

The sensitivity index can be analyzed as follows. The positive sensitivity index shows that an increase in the parameters will lead to increase in the basic reproduction number, while a negative sensitivity index means that an increase in the parameter will lead to a decrease in the basic reproduction number. For example, for $Y_{\beta_m}^{R_0} = 0.5$, increasing the value β_m by 10% increases the reproduction number R_0 by 5%. Thus, increasing natural death rate μ by 10% decreases R_0 by 18.25%.

We also perform sensitivity simulation to verify our sensitivity analysis. The parameter values used in the simulations are given in Table 2. In Figures 4 and 5, we can see that, for the parameter chosen with distinct values of β_f and β_m , respectively, R_0 increases monotonically with both β_m and β_f . This results indicate that increasing β_m and β_f will increase the basic reproduction number R_0 .

5. Numerical Simulation

In this section, we conduct several numerical simulations of model (3). An Adams-type predictor-corrector method [25–27] is applied to solve the numerical solution of the fractional-order model (3). Parameters values used in these

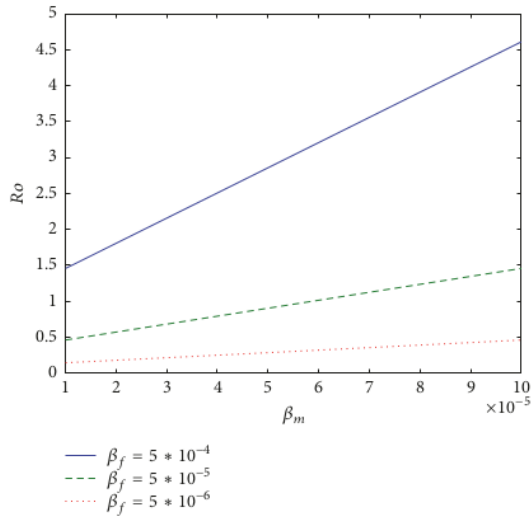


FIGURE 4: Sensitivity of R_0 with respect to β_m for different values of β_f .

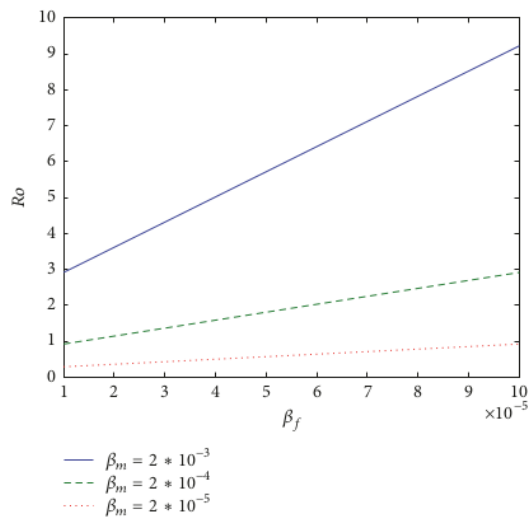


FIGURE 5: Sensitivity of R_0 with respect to β_f for different values of β_m .

simulations could be seen in Table 2. The adopted initial conditions are $(S_m(0), I_m(0), A_m(0), S_f(0), I_f(0), A_f(0)) = (150, 10, 6, 300, 7, 2)$. Here, we take 500 days for the time horizon. The simulations are carried out with varying values of the order of the fractional derivative $\alpha \in [0.5, 1.0]$.

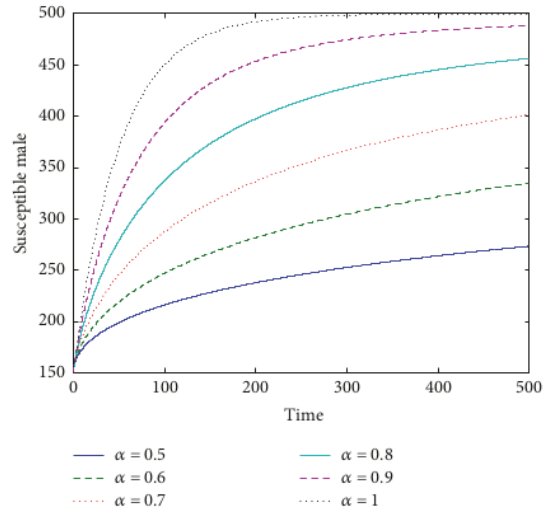


FIGURE 6: Dynamic of nonendemic S_m .

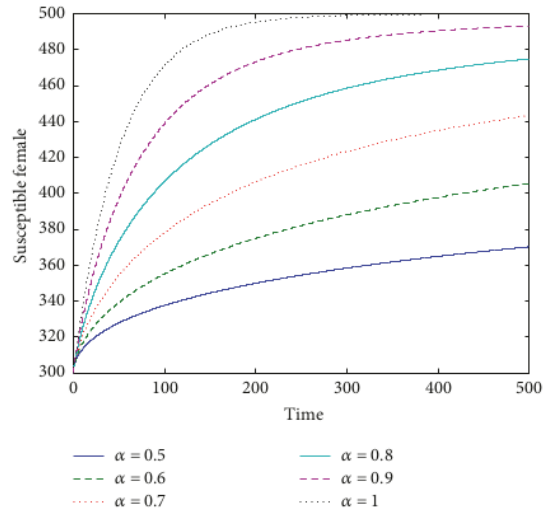


FIGURE 7: Dynamic of nonendemic S_f .

In Figures 6–11, we display the dynamic of the populations when $R_0 < 1$ and in Figures 12–17 when $R_0 > 1$. In each figure six different values of α are employed.

Now, we set $\beta_m = 2 \times 10^{-5}$ and $\beta_f = 5 \times 10^{-5}$ and the remaining of parameters as in Table 2 to simulate Figures 6–11. In this case, the value of R_0 is $R_0 = 0.6521 < 1$ which means that the infection will die out in the population. This condition is confirmed by simulation results in Figures

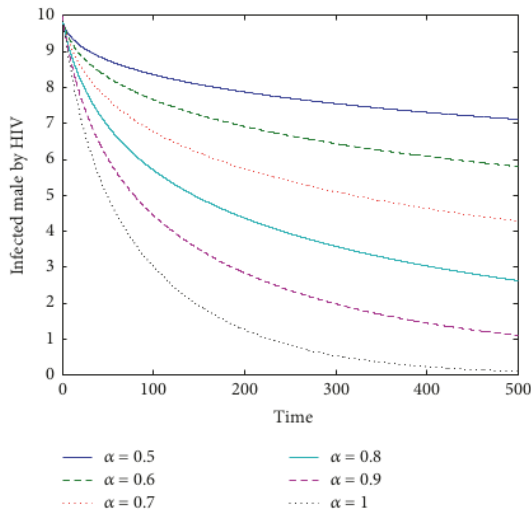


FIGURE 8: Dynamic of nonendemic I_m .

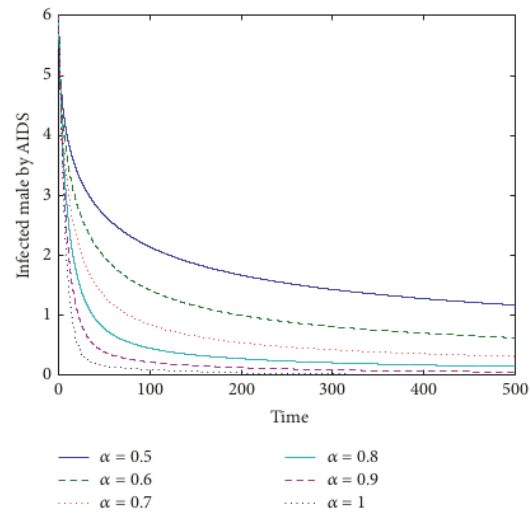


FIGURE 10: Dynamic of nonendemic A_m .

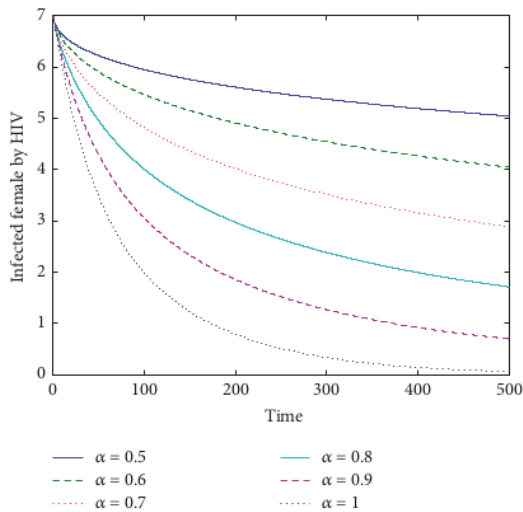


FIGURE 9: Dynamic of nonendemic I_f .

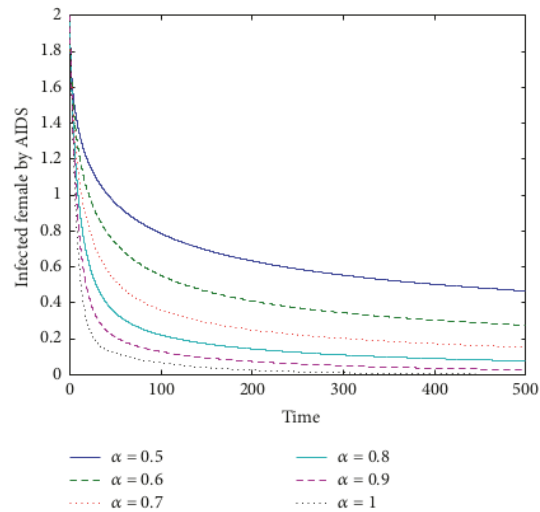


FIGURE 11: Dynamic of nonendemic A_f .

6 and 7, Figures 8 and 9, and Figures 10 and 11 for susceptible male and female populations, respectively, infected by HIV and infected by AIDS. These figures show that the solutions of model (3) are convergent to the disease-free equilibrium. Moreover, we observe that the solutions with higher order α have faster convergence speed compared to the smaller.

Next, we plot in Figures 12–17 the numerical simulations using the parameters as in Table 2. In this condition, the value of R_0 is $R_0 = 65.2051 > 1$ which means that the

infection will persist in the population. In Figures 12 and 13, Figures 14 and 15, and Figures 16 and 17 the dynamics of the susceptible male and female populations, respectively, are seen, infected by HIV and infected by AIDS with different values of α . The figures show that the solutions of model (3) converge to the endemic equilibrium when $R_0 > 1$. Similar to the nonendemic condition, we see that as the order α increases, the convergence of solutions is faster for the endemic condition.

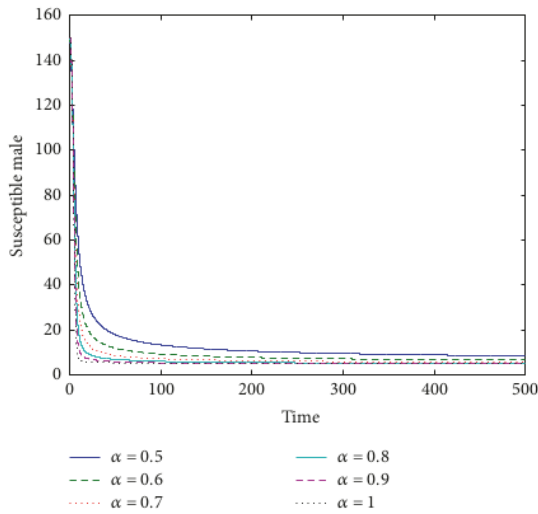


FIGURE 12: Dynamic of endemic S_m .

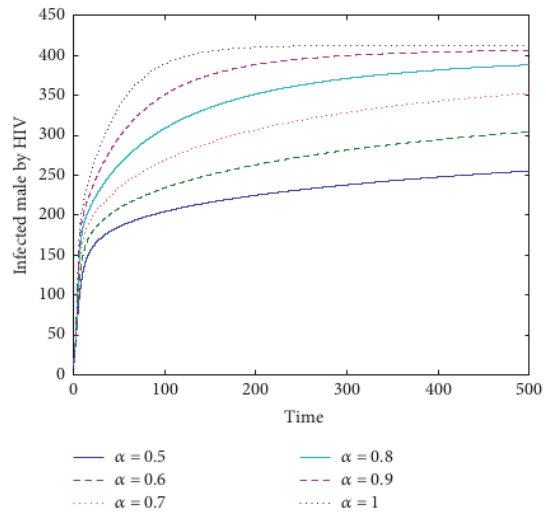


FIGURE 14: Dynamic of endemic I_m .

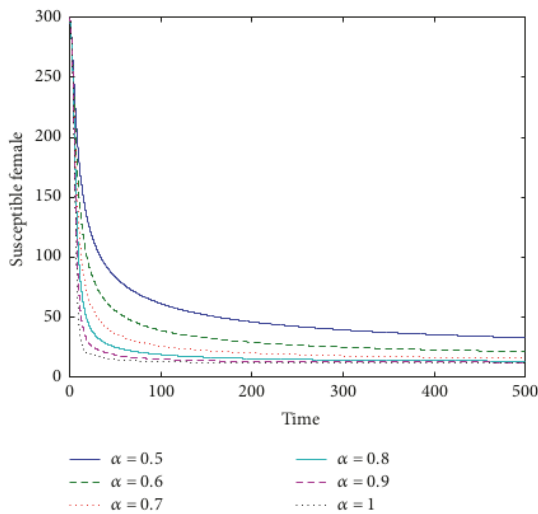


FIGURE 13: Dynamic of endemic S_f .

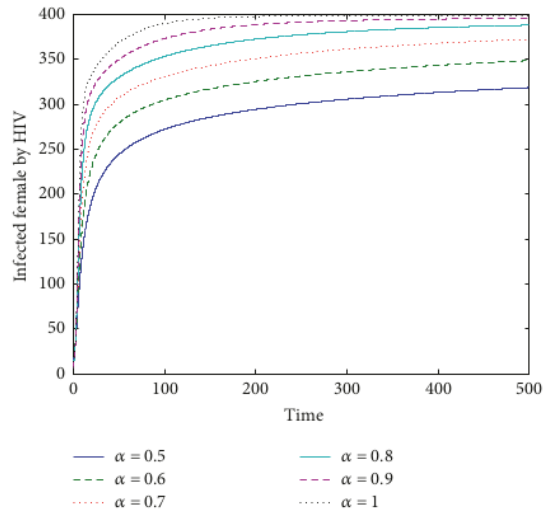


FIGURE 15: Dynamic of endemic I_f .

In Figures 18–23, we depict the dynamic of both male and female populations infected by AIDS for different values of the efficacy of ART treatment (r) for $\alpha = 1$, $\alpha = 0.7$, and $\alpha = 0.5$. For $\alpha = 1$, we observe that the AIDS infected both male and female populations decrease when the value of r is increase. On the contrary, the number of both AIDS infections increases when the efficacy of ART treatment, r , is smaller. The similar behavior is seen for $\alpha = 0.7$ and $\alpha = 0.5$. It is well known that the ART treatment could

improve the quality of HIV infected both male and female patients.

6. Conclusion

In this paper, we have investigated a fractional order of two-sex mathematical model for dynamic HIV, as a generalization of an integer order model, proposed by Kimbir et al. [9]. The basic model in [9] is modified by distinguishing

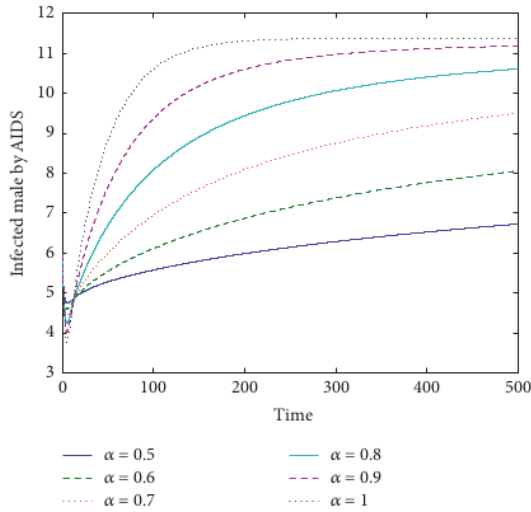


FIGURE 16: Dynamic of endemic A_m .

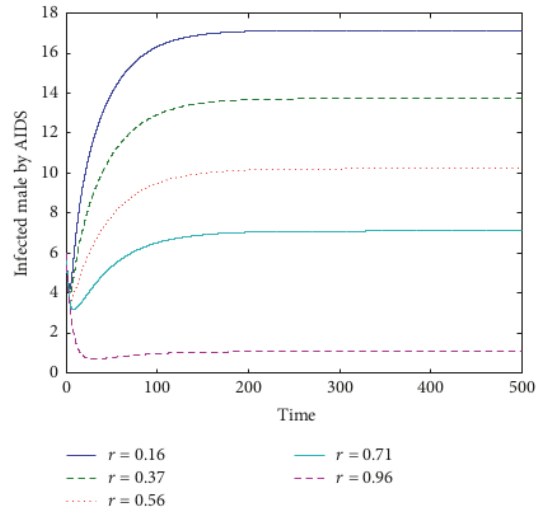


FIGURE 18: Dynamic of A_m with $\alpha = 1$ for various r .

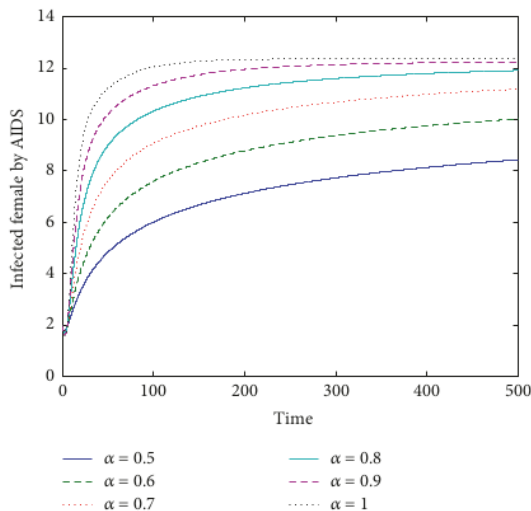


FIGURE 17: Dynamic of endemic A_f .

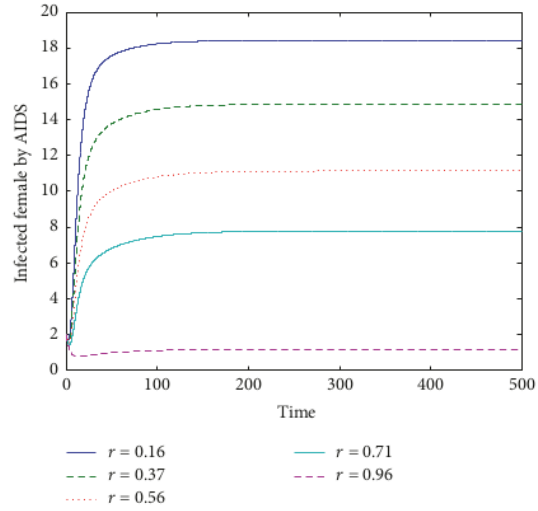


FIGURE 19: Dynamic of A_f with $\alpha = 1$ for various r .

populations infected with HIV and AIDS. We have computed the basic reproduction number (R_0) and proved the stability of equilibriums of the fractional-order model of the HIV infection. Based on the mathematical analysis, the disease-free equilibrium is locally asymptotically stable when $R_0 < 1$ that means the infection will die out in the population. Numerically, the endemic equilibrium tends to be locally asymptotically stable when $R_0 > 1$ which means that the

infection will persist in the population. We also studied analytically and numerically the sensitivity analysis to measure the parameters that have high impact on R_0 . Finally, we have carried out the numerical simulations for different values of the order (α) of the fractional derivative. The simulations results show that the solutions with higher order α have faster convergence compared to the smaller α . We also found that as the efficacy of ART treatment (r) increases there is a

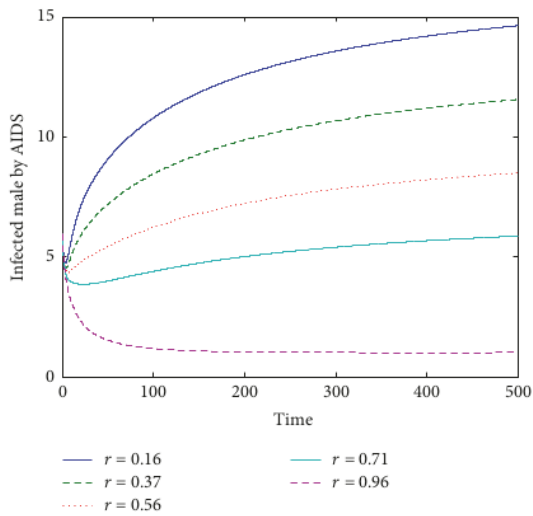


FIGURE 20: Dynamic of A_m with $\alpha = 0.7$ for various r .

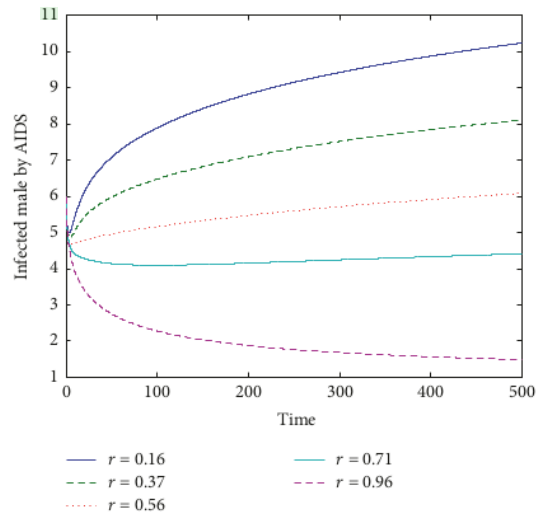


FIGURE 22: Dynamic of A_m with $\alpha = 0.5$ for various r .

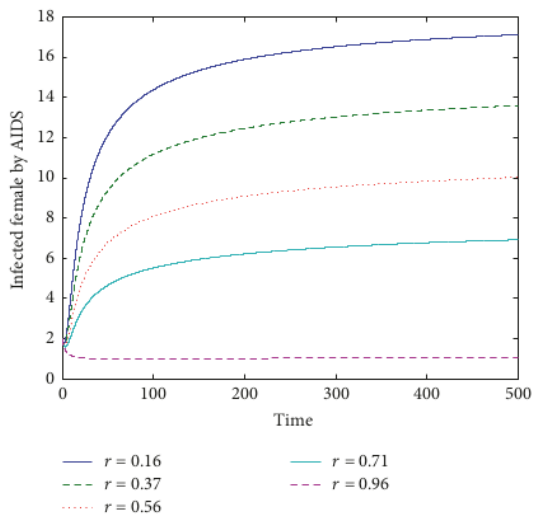


FIGURE 21: Dynamic of A_f with $\alpha = 0.7$ for various r .

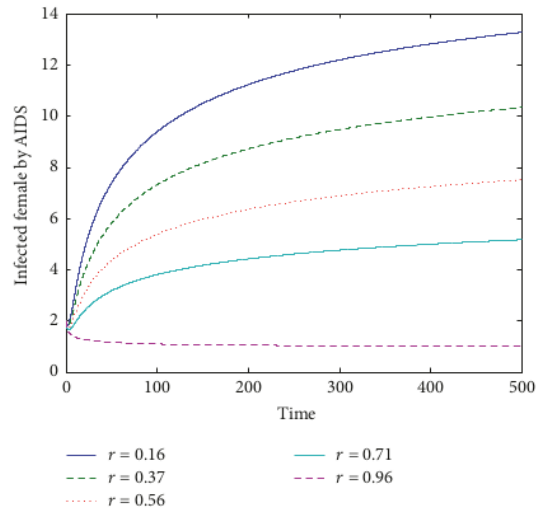


FIGURE 23: Dynamic of A_f with $\alpha = 0.5$ for various r .

corresponding decrease in the number of the AIDS infected both male and female populations for three values of α . These results indicate the effectiveness of the ART treatment to reduce the AIDS infected.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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