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Research Article

Bifurcation and Stabillity Analysis of HIV Transmission Model with Optimal Control

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A mathematical model of HIV transmission is built and studied in this paper. The system's equilibrium is calculated. A next-generation matrix is used to calculate the reproduction number. The novel method is used to examine the developed model's bifurcation and equilibrium stability. The stability analysis result shows that the disease-free equilibrium is locally asymptotically stable if $0 < R_0 < 1$ but unstable if $R_0 > 1$. However, the endemic equilibrium is locally and globally asymptotically stable if $R_0 > 1$ and unstable otherwise. The sensitivity analysis shows that the most sensitive parameter that contributes to increasing of the reproduction number is the transmission rate (β_2) of HIV transmission from HIV individuals to susceptible individuals and the parameter that contributes to the decreasing of the reproduction number is identified as progression rate (η) of HIV-infected individuals to AIDS individuals. Furthermore, it is observed that as we change η from 0.1 to 1, the reproduction number value decreases from 1.205 to 1.189, where the constant value of $\beta_2 = 0.1$. On the other hand, as we change the value of β_2 from 0.1 to 1, the value of the reproduction number increases from 0.205 to 1.347, where the constant value of $\eta = 0.1$. Further, the developed model is extended to the optimal control model of HIV/AIDS transmission, and the cost-effectiveness of the control strategy is analyzed. Pontraygin's Maximum Principle (PMP) is applied in the construction of the Hamiltonian function. Moreover, the optimal system is solved using forward and backward Runge–Kutta fourth-order methods. The numerical simulation depicts the number of newly infected HIV individuals and the number of individuals at the AIDS stage reduced as a result of taking control measures. The cost-effectiveness study demonstrates that when combined and used, the preventative and treatment control measures are effective. MATLAB is used to run numerical simulations.

1. Introduction

Human immunodeficiency virus (HIV) is a retrovirus that attacks the human immune system and causes a highly killing disease called acquired immunodeficiency syndrome (AIDS) [1–6]. HIV was discovered in the early 1980, and it has been persisting in the population [2]. HIV is transmitted through unsafe sex, blood transfusion, breast feeding, materials exposed to the virus, and mother to child during pregnancy [3]. Currently, there is no curing treatment for HIV-infected individuals [4]. In 2018, the number of human individuals living with HIV is estimated to be 37.9 million and the number of dead individuals with AIDS-related disease is 1.2 million. Among HIV-infected individuals, about 62% are tested and taking antiretro therapy (ART) [4]. The data indicate that Africa is the continent that is highly exposed to the human immunodeficiency virus in the world. Particularly in 2018, Ethiopia has about 690,000 peoples living with HIV, 23,000 new people are infected with HIV, and 11,000 individuals dead with AIDS-related disease [5]. To control the transmission of the human immunodeficiency virus, different protective and treatment strategies are used [6]. Some of the strategies used in controlling the transmission and progression of HIV are using condom, be faithful, abstaining, and ART [7]. Even though, different control strategies are used to eradicate and combat the

transmission of HIV in human population, the viruses still become one of the global issues that need attention to save human population from this merciless killing disease.

In this study, we extended the classical SIA model of HIV to the SWIA model of HIV with optimal control problem to identify the best control measures that reduces the transmission and progression of the human immunodeficiency virus along with minimum cost. We have incorporated two control measures in the model and analyzed the cost-effectiveness of the controls.

Mathematical models are efficient tools to describe and predict the transmission dynamics of disease in the population [8, 9].

2. Mathematical Model Formulation

In this study, we extended the SWIA model of HIV into optimal control problem which is significantly different from our previous work in approach and objective of the study. Similar to our previous work, the SWIA model of HIV is described as follows. (i) Susceptible individuals (S): they are individuals who are free of the human immunodeficiency virus but have a chance of possible exposure to the virus having unsafe sexual practices. (ii) Window stage individuals (I): they are new individuals infected with the human immunodeficiency virus but the presence of virus in the blood cannot be verified by the laboratory test. (iii) HIV stage individuals (I): they are pre-AIDS human individuals whose blood test gives the positive results. (iv) AIDS stage individuals (A): they are humans at advanced stage of infection caused by the human immunodeficiency virus and resistant to treatment as a result of weakening the human immune system.

Moreover, the following assumptions are considered in the development of the model:

(i) Human population size is assumed to be nonconstant.

(ii) Individuals are recruited into susceptible population at the recruitment rate λ.

(iii) Human immunodeficiency virus transmitted at the constant transmission rate of β_1, β_2, and β_3 from W, I, and A, respectively.

(iv) The total population size at time t is denoted by $N(t)$ and given by

$$N(t) = S(t) + W(t) + I(t) + A(t). \tag{1}$$

(v) Window stage individuals transfer to HIV stage at the progression rate ρ.

(vi) HIV stage individuals transfer to AIDS stage at the rate of η.

(vii) All humans die naturally at the constant rate μ.

(viii) AIDS stage individuals die at the constant rate δ.

$$\frac{dS}{dt} = \lambda - \frac{S}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - \mu S, \tag{2}$$

$$\frac{dW}{dt} = \frac{S}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - (\rho + \mu)W, \tag{3}$$

$$\frac{dI}{dt} = \rho W - (\eta + \mu)I, \tag{4}$$

$$\frac{dA}{dt} = \eta I - (\delta + \mu)A. \tag{5}$$

with $S(0)>0$, $W(0)>0$, $I(0)>0$, and $A(0)>0$.

3. Mathematical Analysis of the Model

3.1. Well-Posedness of the Model

3.1.1. Invariant Region

Theorem 1. *The set $\Omega \subset \mathfrak{R}_+^4$ is the invariant region of boundedness if for all initial solutions $(S(0), W(0), I(0), A(0)) \in \Omega$ and for all $t \geq 0$, then $(S(t), W(t), I(t), A(t)) \in \Omega$. That is,*

$$\Omega = \left\{ (S(t), W(t), I(t), A(t)) : S(t), W(t), I(t), A(t) \in \mathfrak{R}_+^4, \forall t \geq 0 \right\}. \tag{6}$$

Proof. Considering model (4) and adding all corresponding terms on the left of equality and terms on right of equality, we get

$$\frac{dN}{dt} \leq \lambda - \mu N + \delta A. \tag{7}$$

Solving the preceding inequality and considering the expression as time t gets larger, we obtain

$$N(t) \leq \frac{\lambda}{\mu}. \tag{8}$$

The preceding inequality shows that all solution variables are bounded in $\mathfrak{R}_+^4$. Therefore, using equation (4), $\Omega \subset \mathfrak{R}_+^4$ is the invariant set of solutions such that

$$\Omega = \left\{ (S(t), W(t), I(t), A(t)) : S(t), +W(t) + I(t) + A(t) \leq \frac{\lambda}{\mu}, \forall t \geq 0 \right\}. \tag{9}$$

□

3.1.2. Positivity of Solutions

Theorem 2. *All solutions of model (4) are nonnegative for all time t provided that initial conditions are nonnegative.*

Proof. Taking the first equation of model (4), we have

$$\frac{dS}{dt} = \lambda - \frac{S(\beta_1 W + \beta_2 I + \beta_3 A)}{N} - \mu S. \tag{10}$$

Neglecting the term λ, the foregoing equation is reduced to the next inequality

$$\frac{dS}{S} \geq -\left(\frac{(\beta_1 W + \beta_2 I + \beta_3 A)}{N} + \mu\right)dt. \tag{11}$$

Solving the foregoing inequality over time interval $[0, t]$, we get

$$S(t) \geq S(0)e^{-\mu t - \int_0^t ((\beta_1 W(\xi) + \beta_2 I(\xi) + \beta_3 A(\xi))/N(\xi))d\xi}. \tag{12}$$

Since the initial condition $S(0)$ and the exponential expression $e^{-\mu t - \int_0^t ((\beta_1 W(\xi) + \beta_2 I(\xi) + \beta_3 A(\xi))/N(\xi))d\xi}$ are nonnegative, the solution variable $S(t)$ is nonnegative for all time t. Similarly, other solution variables are nonnegative. □

3.1.3. Existence and Uniqueness of Solutions

Theorem 3. *The solutions of model (4) exist and are unique in* $\mathfrak{R}_+^4$.

Proof. Since the expression on the right-hand side of model (4) is bounded and continuously differentiable, the proof directly follows from Cauchy–Lipschitz theorem (see [10]).

Therefore, the formulated model (4) is mathematically well-posed and biologically acceptable. □

3.2. Equilibriums of the Model

3.2.1. Disease-Free Equilibrium (DFE). The disease-free equilibrium (E_0) is a point in the system where there is no disease in the population. The computed disease-free equilibrium of the model one is given by

$$E_0 = (S^0, 0, 0, 0), \tag{13}$$

where $S^0 = \lambda/\mu$.

3.2.2. Endemic Equilibrium (EE). The endemic equilibrium of the model is the point where the disease persists in the population. The computed endemic equilibrium of model (4) is given by

$$E_1 = (S^*, W^*, I^*, A^*), \tag{14}$$

where $S^* = ((a+b+c)\lambda/R_0 + \mu(a+b+c) - 1), W^* = (\lambda/\rho + \mu)(R_0 - 1/R_0 + \mu(a+b+c) - 1), I^* = (\rho W^*/\eta + \mu), A^* = (\eta I^*/\delta + \mu), a = (1/\rho + \mu), b = (\rho/(\rho + \mu)(\eta + \mu))$, and $c = (\eta\rho/(\rho + \mu)(\eta + \mu)(\delta + \mu))$.

3.3. Basic Reproduction Number (R_0). The basic reproduction number is the average number of infected individuals produced by one infectious individual in the susceptible population during entire period of infection [11]. We have computed the basic reproduction number using the next-generation matrix employed in [12]. Accordingly, from model (4), let $f = \begin{pmatrix} (S(\beta_1 W + \beta_2 I + \beta_3 A)/N) \\ 0 \\ 0 \end{pmatrix}$ represent the newly infected individuals in the infectious compartments and $v = \begin{pmatrix} (\rho + \mu)W \\ -\rho W + (\eta + \mu)I \\ -\eta I + (\delta + \mu)A \end{pmatrix}$ be the remaining terms of infected compartments. So that, the Jacobian matrices obtained from f and v at the disease-free equilibrium are denoted by F and V, respectively. So that,

$$F = \begin{pmatrix} \beta_1 & \beta_2 & \beta_3 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \rho + \mu & 0 & 0 \\ -\rho & \eta + \mu & 0 \\ 0 & -\eta & \delta + \mu \end{pmatrix}. \tag{15}$$

The next-generation matrix FV^{-1} is computed as follows:

$$FV^{-1} = \begin{pmatrix} \frac{\beta_1}{\rho+\mu} + \frac{\beta_2\rho}{(\rho+\mu)(\eta+\mu)} + \frac{\beta_3\eta\rho}{(\rho+\mu)(\eta+\mu)(\delta+\mu)} & \frac{\beta_2}{(\eta+\mu)} + \frac{\beta_3\eta}{(\eta+\mu)(\delta+\mu)} & \frac{\beta_3}{\delta+\mu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \tag{16}$$

The computed eigenvalues of the foregoing next-generation matrix are given by

$$\lambda_1 = \frac{\beta_1}{\rho+\mu} + \frac{\beta_2\rho}{(\rho+\mu)(\eta+\mu)} + \frac{\beta_3\eta\rho}{(\rho+\mu)(\eta+\mu)(\delta+\mu)}, \quad \lambda_2 = 0,\ \lambda_3 = 0. \tag{17}$$

The basic reproduction number $R_0 = \rho(FV^{-1})$ and given by

$$R_0 = \frac{\beta_1}{\rho+\mu} + \frac{\beta_2\rho}{(\rho+\mu)(\eta+\mu)} + \frac{\beta_3\eta\rho}{(\rho+\mu)(\eta+\mu)(\delta+\mu)}. \tag{18}$$

3.4. Stability Analysis of Disease-Free Equilibrium

Theorem 4. *The disease-free equilibrium becomes locally asymptotically stable if $R_0 < 1$ and becomes unstable if $R_0 > 1$.*

Proof. To determine the local stability of the disease-free equilibrium, we constructed a Jacobian (J) from model (2) at the disease-free equilibrium as follows:

$$J = \begin{pmatrix} -\mu & -\beta_1 & -\beta_2 & -\beta_3 \\ 0 & \beta_1 - (\rho+\mu) & \beta_2 & \beta_3 \\ 0 & \rho & -(\eta+\mu) & 0 \\ 0 & 0 & \eta & -(\delta+\mu) \end{pmatrix}. \tag{19}$$

The eigenvalues of the above matrix can be obtained by solving the characteristic equation as follows:

$$\det(J - \lambda I) = 0. \tag{20}$$

The characteristic equation can be written as

$$(\lambda+\mu)\left(a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3\right) = 0, \tag{21}$$

where $a_0 = 1$, $a_1 = \eta + \rho + \delta + 3\mu - \beta_1$, $a_2 = \eta\delta + 2\eta\mu + 2\delta\mu + \eta(\eta+\delta+2\mu) + 3\mu^2 - \beta_1(\eta+\delta+2\mu) - \beta_2$, and $a_3 = \eta\mu^2 + \delta\mu^2 + \rho\mu^2 + \mu^3 + \eta\delta\mu + \eta\delta\rho + \eta\mu\rho + \delta\mu\rho - \beta_1(\mu^2 + \eta\delta + \eta\mu + \delta\mu) - \beta_2(\delta\rho + \mu\rho) - \beta_3\eta\rho$.

By the Hurwitz–Routh principle, all eigenvalues of the characteristic equation are negative if and only if the following conditions are satisfied:

$$\begin{aligned} a_0 &> 0, \\ a_1 a_2 &> a_3. \end{aligned} \tag{22}$$

Therefore, by stability theory of differential equations, the disease-free equilibrium becomes locally asymptotically stable if $0 < R_0 < 1$ and becomes unstable if $R_0 > 1$. □

Theorem 5. *The disease-free equilibrium of the constructed model (4) is globally asymptotically unstable if $0 < R_0 < 1$ and unstable otherwise.*

Proof. To prove global stability of the disease-free equilibrium, we apply the methods applied in [13] as follows.

Accordingly, let $X \in \mathbb{R}^1$ be uninfected individuals in class (S) and $Y \in \mathbb{R}^3$ be individuals in infected class $(I,\ U,\ A)$. Hence, we write model (4) as follows:

$$\begin{aligned} \frac{dX}{dt} &= H(X,Y), \\ \frac{dY}{dt} &= G(X,Y), \\ G(X,0) &= 0. \end{aligned} \tag{23}$$

The disease-free equilibrium of the foregoing system is computed as

$$E_0^1 = \left(X^0, 0\right). \tag{24}$$

To guarantee global stability, the method we applied must meet conditions H1 and H2 stated as follows:

H1. For $(dX/dt) = H(X,0)$, X^0 is globally asymptotically stable

H2. $G(X,Y) = PY - \widehat{G}(X,Y)$, $\widehat{G}(X,Y) \geq 0$ for $(X,Y) \in \Omega$

Here, $P = D_Y G(X,0)$ be the Metzler matrix and Ω is a region where solutions are acceptable. □

Theorem 6. *The disease-free equilibrium of model (4) is globally asymptotically stable in a region Ω if $R_0 < 1$ and unstable whenever $R_0 > 1$ provided that the stated two conditions H1 and H2 are satisfied.*

Proof. Considering model (4), we have

$$H(X,0) = \lambda - \mu S = H(S,0). \tag{25}$$

Putting $H(X,0) = 0$ and solving, we obtain $S = (\lambda/\mu)$. Hence, $X^0 = (\lambda/\mu, 0)$.

We observe that X^0 is the globally asymptotically stable equilibrium of equation as follows:

$$\frac{dX}{dt} = H(X,0). \tag{26}$$

Further, considering the infected compartments of model (27), we have

$$\frac{dS}{dt} = \lambda - \frac{S}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - \mu S,$$

$$\frac{dW}{dt} = \frac{S}{N}(\beta_1 W + \beta_2 I + \beta_3 A) - (\rho + \mu)W,$$

$$\frac{dI}{dt} = \rho W - (\eta + \mu)I,$$

$$\frac{dA}{dt} = \eta I - (\delta + \mu)A,$$

$$G(X,Y) = \begin{bmatrix} \beta_1 W + \beta_2 I + \beta_3 A - (\rho + \mu) & 0 & 0 \\ \rho & -(\eta + \mu) & 0 \\ 0 & \eta & -(\delta + \mu) \end{bmatrix} \begin{bmatrix} W \\ I \\ A \end{bmatrix} - \begin{bmatrix} \beta_1 W + \beta_2 I + \beta_3 A - \frac{S}{N}(\beta_1 W + \beta_2 I + \beta_3 A) \\ 0 \\ 0 \end{bmatrix}. \tag{27}$$

Further, at the disease-free equilibrium, the preceding equation is reduced to the form as follows:

$$G(X,Y) = \begin{bmatrix} -(\rho + \mu) & 0 & 0 \\ \rho & -(\eta + \mu) & 0 \\ 0 & \eta & -(\delta + \mu) \end{bmatrix} \begin{bmatrix} W \\ I \\ A \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}. \tag{28}$$

Now, comparing the required condition and the preceding equation, we obtain

$$P = \begin{bmatrix} -(\rho + \mu) & 0 & 0 \\ \rho & -(\eta + \mu) & 0 \\ 0 & \eta & -(\delta + \mu) \end{bmatrix},$$

$$Y = \begin{bmatrix} W \\ I \\ A \end{bmatrix}, \tag{29}$$

$$\widehat{G}(X,Y) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}.$$

Now, we observe that $G(X,Y) = PY - \widehat{G}(X,Y)$, where $\widehat{G}(X,Y) \geq 0$, $\forall X, Y$.

Therefore, the disease-free equilibrium E_0 is globally asymptotically stable if $R_0 < 1$. □

3.5. Bifurcation and Stability Analysis of Endemic Equilibrium. In this subsection, we simulate the endemic equilibrium versus reproduction number to identify the kind of bifurcation that occurs at the point $R_0 = 1$ and to determine the stability behavior of equilibriums if $R_0 < 1$ and $R_0 > 1$. The simulation of the endemic equilibrium (S^*, W^*, I^*, A^*) versus R_0 is given in Figure 1.

Theorem 7. *The endemic equilibrium of model (2) undergoes forward bifurcation at* $R_0 = 1$.

Proof. (see [3, 14] and Figure 1). □

Theorem 8. *The endemic equilibrium* E_1 *is globally asymptotically positively stable if* $R_0 > 1$.

Proof. (see [3, 14] and Figure 1). □

Theorem 9. *The endemic equilibrium of model (27) is locally asymptotically stable if* $R_0 > 1$ *and unstable if* $0 < R_0 < 1$.

Proof. We have already computed the endemic equilibrium E_1 as

$$E_1 = (S^*, W^*, I^*, A^*), \tag{30}$$

where $S^* = ((a+b+c)\lambda/R_0 + \mu(a+b+c) - 1)$, $W^* = (\lambda/\rho + \mu)(R_0 - 1/R_0 + \mu(a+b+c) - 1)$, $I^* = (\rho W^*/\eta + \mu)$, $A^* = (\eta I^*/\delta + \mu)$, $a = (1/\rho + \mu)$, $b = (\rho/(\rho + \mu)(\eta + \mu))$, and $c = (\rho\eta/(\rho + \mu)(\eta + \mu)(\delta + \mu))$.

Clearly, the endemic equilibrium exists only if $R_0 > 1$. Therefore, using center manifold theory stated in [15, 16], Figure 1, and stability theory of differential equations, the endemic equilibrium of model (27) is locally asymptotically stable if $R_0 > 1$ and unstable if $R_0 < 1$. □

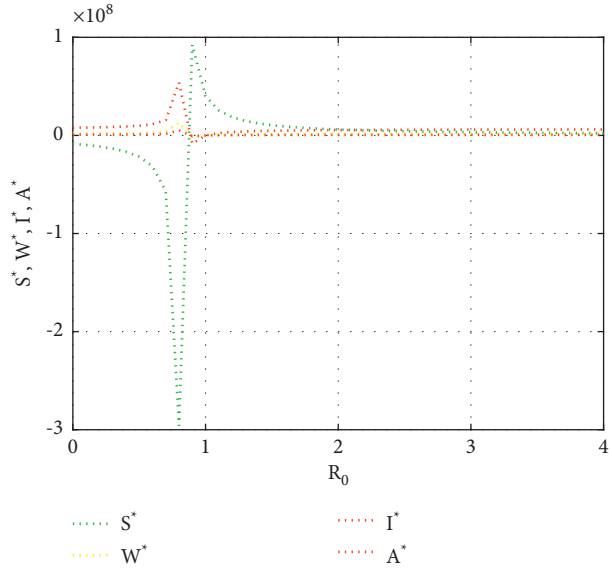

Figure 1: Simulation of the endemic equilibrium versus reproduction number.

3.6. Sensitivity Analysis. In this subsection, we determine the most sensitive parameter that contributes in increasing (decreasing) the reproduction number using the normalized forward sensitivity index stated in [17]. That is, the normalized forward sensitive index of R_0 with respect to parameter p is denoted by $Y_p^{R_0}$ and defined as

$$Y_p^{R_0} = \frac{\partial R_0}{\partial p}\frac{p}{R_0}. \tag{31}$$

From our earlier computations, R_0 is given by

$$R_0 = \frac{\beta_1}{\rho+\mu} + \frac{\beta_2\rho}{(\rho+\mu)(\eta+\mu)} + \frac{\beta_3\eta\rho}{(\rho+\mu)(\eta+\mu)(\delta+\mu)}. \tag{32}$$

To determine the most sensitive parameter in the model, we perform the following computations and results are given in Table 1:

$$\begin{aligned}
Y_{\beta_1}^{R_0} &= \frac{\partial R_0}{\partial \beta_1}\frac{\beta_1}{R_0} = \frac{\beta_1}{(\rho+\mu)R_0},\\
Y_{\beta_2}^{R_0} &= \frac{\partial R_0}{\partial \beta_2}\frac{\beta_2}{R_0} = \frac{\rho\beta_2}{(\rho+\mu)(\eta+\mu)R_0},\\
Y_{\beta_3}^{R_0} &= \frac{\partial R_0}{\partial \beta_3}\frac{\beta_3}{R_0} = \frac{\eta\rho\beta_3}{(\rho+\mu)(\eta+\mu)(\delta+\mu)R_0},\\
Y_{\rho}^{R_0} &= \frac{\partial R_0}{\partial \rho}\frac{\rho}{R_0} = \left(-\frac{\beta_1}{(\rho+\mu)^2} + \frac{\beta_2\mu}{(\rho+\mu)^2(\eta+\mu)} + \frac{\beta_3\eta\mu}{(\rho+\mu)^2(\eta+\mu)(\delta+\mu)}\right)\frac{\rho}{R_0},\\
Y_{\eta}^{R_0} &= \frac{\partial R_0}{\partial \eta}\frac{\eta}{R_0} = \left(-\frac{\beta_2\rho}{(\eta+\mu)^2(\rho+\mu)} + \frac{\beta_3\rho\mu}{(\eta+\mu)^2(\rho+\mu)(\delta+\mu)}\right)\frac{\eta}{R_0},\\
Y_{\mu}^{R_0} &= \frac{\partial R_0}{\partial \mu}\frac{\mu}{R_0} = \left(-\frac{\beta_1}{(\rho+\mu)^2} - \frac{\beta_2\rho(\eta+\rho+2\mu)}{(\rho+\mu)^2(\eta+\mu)^2} - \frac{\beta_3\eta\rho((\eta+\delta+2\mu)(\rho+\mu)) + (\eta+\mu)(\delta+\mu)}{(\rho+\mu)^2(\eta+\mu)^2(\delta+\mu)^2}\right)\frac{\mu}{R_0},\\
Y_{\delta}^{R_0} &= \frac{\partial R_0}{\partial \delta}\frac{\delta}{R_0} = -\frac{\beta_3\eta\rho\delta}{(\rho+\mu)(\eta+\mu)(\delta+\mu)^2R_0}.
\end{aligned} \tag{33}$$

Table 1: Computed sensitivity index value.

Parameter	Value	Sensitivity index
β_1	0.2	+0.23
β_2	0.16	+0.768
β_3	0.0024	+0.001
ρ	0.5	−0.19
η	0.1	−1.28
μ	0.02	−0.011
δ	1	−0.001

4. Optimal Control of HIV Model

In this section, we analyze the optimal control model (2) to identify the best control strategy that reduces the number of AIDS individuals and minimizes the total cost used in during the interventions. The incorporated control strategies are described as follows:

(i) *Preventive Control* (u_1). HIV prevention measures include HIV-AIDS education, condom usage, abstinence, and faithfulness.

(ii) *Treatment Control* (u_2). ART treatment reduces the number of virus in human blood, and as a result, the number of individuals that progress to AIDS stage will be reduced. Our goal is to minimize the number of AIDS individuals by effectively using the control measures along with minimum cost. The normalized optimal control model is given by

$$\begin{aligned}
\frac{ds}{dt} &= b(1-s) - (1-u_1)s(\beta_1 w + \beta_2 i + \beta_3 a) + s\delta a,\\
\frac{dw}{dt} &= (1-u_1)s(\beta_1 w + \beta_2 i + \beta_3 a) - (\rho + b)w + w\delta a,\\
\frac{di}{dt} &= \rho w - ((1-u_2)\eta + b)i + i\delta a,\\
\frac{da}{dt} &= (1-u_2)\eta i - (b+\delta)a + \delta a^2.
\end{aligned} \tag{34}$$

To characterize the optimal levels of the controls, we define the lebesgue measurable control set U as

$$U = \{u_1, u_2 : 0 \le u_1 \le 1,\ 0 \le u_2 \le 1,\ 0 \le t \le T\}. \tag{35}$$

The 0 value of control measure means that there are no control measures taken against HIV/AIDS prevention or treatment [18]. The value of control measure indicates that full control measure is taken against the HIV/AIDS prevention or treatment. The objective functional or cost functional that describes the consumed total cost to minimize the number of window individuals and AIDS individuals is defined as

$$J = \min \int_0^{t_f} \left(c_1 w + c_2 a + \frac{1}{2}\left(w_1 u_1^2 + w_2 u_2^2\right)\right) dt, \tag{36}$$

where the coefficients c_1 and c_2 of state variables are constants and coefficients w_1 and w_2 are the measure of the consumed costs of intervention associated to controls u_1 and u_2, respectively [7]. All constant coefficients are positive [18]. Our aim is to obtain the optimal controls that minimize new infected individuals and reduces the number of AIDS individuals along with minimum cost of interventions. Since cost is nonlinear, we assume quadratic expression $(1/2)w_i u_i^2$ where $i = 1, 2$.

4.1. Existence and Description of Optimal Control Solution

Theorem 10 (existence of optimal solution). *There exist optimal controls u_1^* and u_2^* and state variables s^*, w^*, i^*, and a^* for the initial value problems (34) and (39) that minimize $J(u_1, u_2)$ over U.*

Proof. The admissible control set U is determined using Fleming and Rishel's theorem.

(i) The solution set of (34) and (39) with corresponding control function be nonempty

(ii) The state system is a linear function of control variables and coefficients depending on state variables and time

(iii) The integrand $L = c_1 w + c_2 a + (1/2)(w_1 u_1^2 + w_2 u_2^2)$ of objective functional J is convex on U and $L \ge \alpha|(u_1, u_2)|^\beta - \gamma$, where $\alpha > 0$ and $\beta > 1$

To verify condition (i), we use [7]. If the functions of state equations are continuous, bounded, and Lipschitz in state variables, then to every admissible control U, there is unique solution. The total population size is bounded, the state variables are bounded, and the partial derivatives of functions constructed from state equations are bounded. Therefore, condition (i) is satisfied. Condition (ii) holds by observing the linearity of the state equation in controls u_1 and u_2. Condition (iii) follows from definition that any quadratic function, linear, and constant functions are convex. Hence, L is convex on U. Next, we show boundedness of L.

Since $w_1 u_2^2 \le w_2$ and $(1/2)w_1 u_2^2 \le (1/2)w_2^2$ for $u_2 \in [0, 1]$, then $L = c_1 w + c_2 a + (1/2)(w_1 u_1^2 + w_2 u_2^2) \ge (1/2)(w_1 u_1^2 + w_2 u_2^2) - (1/2)w_2^2$.

$$\begin{aligned}
&\Rightarrow L \ge \min\left(\frac{w_1}{2}, \frac{w_2}{2}\right)\left(u_1^2 + u_2^2\right) - \frac{1}{2}w_2^2,\\
&\Rightarrow L \ge \min\left(\frac{w_1}{2}, \frac{w_2}{2}\right)u_1,\ {u_2}^2 - \frac{1}{2}w_2^2.
\end{aligned} \tag{37}$$

Thus, $L \ge \alpha|(u_1, u_2)|^\beta - \gamma$, where $\alpha = \min((w_1/2), (w_2/2))$, $\beta = 2$, and $\gamma = (1/2)w_2^2$.

Applying Pontryagin's Maximum Principle (PMP) as in [7, 19], we obtained the necessary conditions to be fulfilled by optimal control pairs. Therefore, in order to construct the optimal system that minimize the cost functional, we defined the Hamiltonian function as follows:

$$H = c_1 w + c_2 a + \frac{1}{2}\left(w_1 u_1^2 + w_2 u_2^2\right) + \lambda_1 [b(1-s) - (1-u_1)s(\beta_1 w + \beta_2 i + \beta_3 a) + s\delta a]$$
$$+ \lambda_2 [(1-u_1)s(\beta_1 w + \beta_2 i + \beta_3 a) - (\rho + b)w + w\delta a] \tag{38}$$
$$+ \lambda_3 [\rho w - ((1-u_2)\eta + b)i + i\delta a] + \lambda_4 \left[(1-u_2)\eta i - (b+\delta)a + \delta a^2\right],$$

where λ_i, $i = 1, 2, 3, 4$ are adjoint variable functions corresponding to state variables s, w, i, and a determined as follows [4] for existence of optimal control pairs.

Variables λ_i, $i = 1, 2, 3, 4$ such that

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial s} = (1-u_1)(\beta_1 w + \beta_2 i + \beta_3 a)(\lambda_1 - \lambda_2) + (b - \delta a)\lambda_1,$$
$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial w} = -c_1 + (1-u_1)s\beta_1(\lambda_1 - \lambda_2) + \rho(\lambda_2 - \lambda_3) + (b - \delta a)\lambda_2,$$
$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial i} = (1-u_1)s\beta_2(\lambda_1 - \lambda_2) + (1-u_2)\eta(\lambda_3 - \lambda_4) + (b - \delta a)\lambda_3, \tag{39}$$
$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial a} = -c_2 + (1-u_1)s\beta_3(\lambda_1 - \lambda_2) - s\delta\lambda_1 - w\delta\lambda_2 + i\delta\lambda_3 + (b + \delta - 2\delta a)\lambda_4.$$

With transversality conditions $\lambda_i(t_f) = 0$, $i = 1, 2, 3, 4$. Further, we obtained the control set $\{u_1^*(t), u_2^*(t)\}$ such that $u_1^*(t) = \max\{0, \min\{1, u_1^*\}\}, u_2^*(t) = \max\{0, \min\{1, u_2^*\}\}$, where $u_1^* = (s(\beta_1 w + \beta_2 i + \beta_3 a)(\lambda_2 - \lambda_1)/w_1)$ and $u_2^* = (\eta i(\lambda_4 - \lambda_3)/w_2)$. □

5. Numerical Simulations of Optimal Control Solutions

Numerical simulations are very important to describe the behavior of populations qualitatively. Numerical solution of optimal control problem is simulated by assuming parameter values logically as described in Table 2.

So far, we have discussed the optimal control problem analytically. In this section, to validate our analytical findings, we perform numerical simulations to analyze the minimum cost required during application of control measures. So, we solve control systems (34) and (39) numerically by using the value of parameters assigned in Table 2 and initial population sizes along with fixed final time $t_f = 10$ years. Assume the initial population size in the proportionality form as $s = 0.6, w = 0.1, i = 0.2$, and $a = 0.1$. Also, we assumed constants in objective functional as $c_1 = 2, c_2 = 3, w_1 = 10$, and $w_2 = 20$.

5.1. Cost-Effectiveness Analysis. In this section, we analyze cost-effectiveness of control strategies to rank them in terms of their cost. To identify the best control strategies along with minimum coast, we apply the method applied in other researchers work in [20]. They had stated a formula as follows:

$$\text{incremental cost} - \text{effectiveness ratio (ICER)} = \frac{\text{difference in costs between strategies}}{\text{difference in health effects between strategies}}. \tag{40}$$

Based on the description of controls, infectious averted, and total cost given in Table 3, we compute the incremental cost-effectiveness ratio (ICER) as

$$\text{ICER}(1) = \frac{2.6470}{0.00975} = 271.4872, \tag{41}$$

$$\text{ICER}(2) = \frac{2.6931 - 2.6470}{0.41184 - 0.00975} = 0.1147. \tag{42}$$

Table 2: Parameter and value assigned.

Parameter	Value	Source
λ	800000	Assumed
β_1	0.2	Assumed
β_2	0.16	Assumed
β_3	0.0024	Assumed
η	0.1	[18, 9]
δ	1	[18, 9]
ρ	0.5	Assumed
b	0.03	Assumed
μ	0.02	[9]

Table 3: Description of controls, infectious averted, and cost.

Strategies	Description	Total infectious averted	Total cost (USD)
1	Prevention control	0.00975	2.6470
2	Treatment control	0.41184	2.6931
3	Prevention and treatment controls	0.00879	2.644

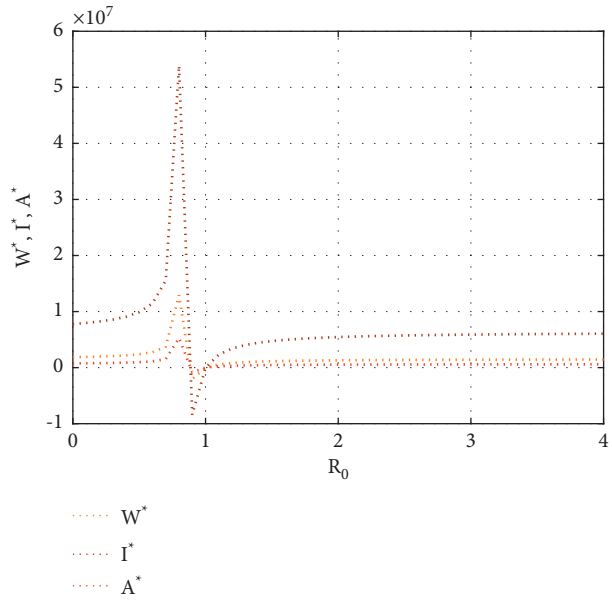

Figure 2: The simulations of HIV-infected populations versus the reproduction number.

Comparing ICER(2) < ICER(1), thus select strategy (2) and ignore strategy (1) as it is expensive and less effective. Again, we compare ICER (2) and ICER (3) by first computing ICER (2) and ICER (3) as follows:

$$\text{ICER}(2) = \frac{2.6931}{0.41184} = 6.5392, \tag{43}$$

$$\text{ICER}(3) = \frac{2.644 - 2.6931}{0.00879 - 0.41184} = 0.1218. \tag{44}$$

Comparing the computed values ICER(3) < ICER(2) shows that strategy (2) is more expensive and less effective than strategy (3). Therefore, we conclude that using both preventive and treatment control strategies is more effective than using controls separately toward prevention and controlling of the human immunodeficiency virus.

6. Results and Discussion

The optimum control model of HIV/AIDS is numerically solved in this paper using Runge–Kutta fourth-order forward and backward methods, as well as MATLAB software. Simulation in Figure 1 shows that forward bifurcation occurs at $R_0 = 1$ and the endemic equilibrium exists only if $R_0 > 1$. Thus, the disease persists in the population if and only if the average number of infected individuals produced by an infectious individual in the entire period of infection is greater than one. Also, the endemic equilibrium is globally asymptotically stable if $R_0 > 1$ and unstable if $R_0 < 1$. Figure 2 shows the simulation of the infected individuals equilibrium versus reproduction number; the size of all HIV-infected individuals becomes zero at $R_0 = 1$, and HIV-infected individuals survive

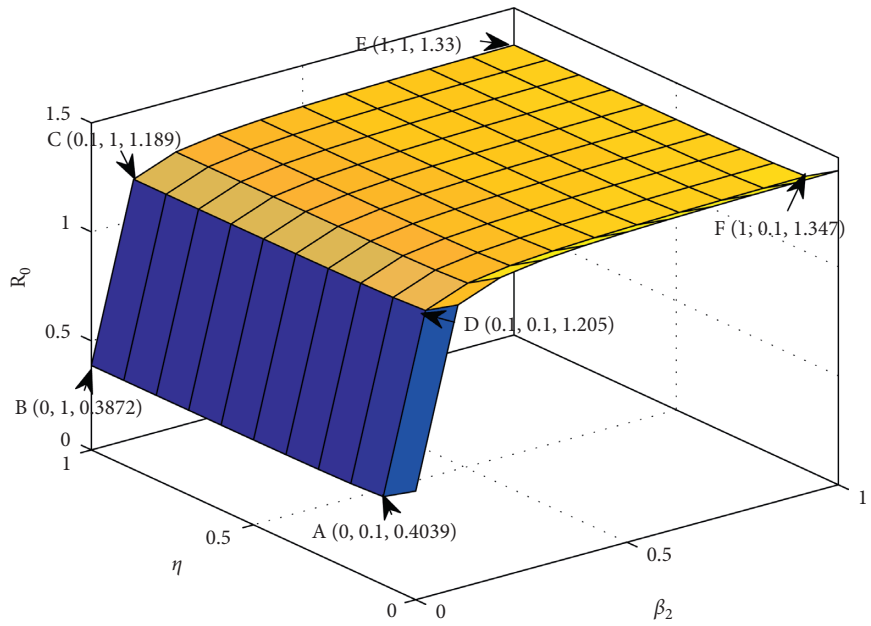

Figure 3: The simulation of the reproduction number versus parameters β_2 and η.

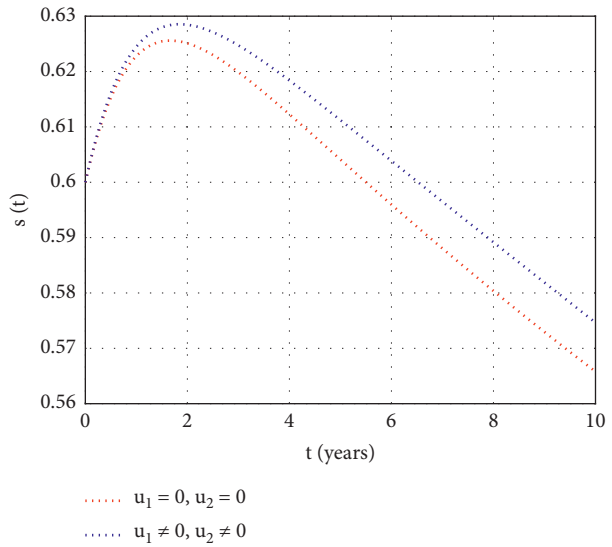

Figure 4: Simulation of susceptible population size without and with controls.

if $R_0 > 1$. A reproduction number's sensitivity to highly sensitive parameters is investigated in Figure 3. The value of the reproduction number drops as we raise the parameter with a negative sensitive index and increases as we increase the parameter with a positive sensitivity index (see, Table 1). The inclusion of preventative and treatment control measures spared more susceptible persons from becoming infected with the human immunodeficiency virus, as shown in Figure 4. The presence of control measures lowered the number of window persons, as shown in Figure 5. The existence of preventative and treatment control measures lowered the number of HIV patients who were transitioned to acquired immunodeficiency syndrome (AIDS), as shown in Figure 6. Figure 7 illustrates that the availability of preventative and treatment control measures has no discernible effect on the number of people living with AIDS. Figure 8 indicates that the preventative control measure falls from the start to the end of the time, whereas the treatment control measure climbs for about 5 years before gradually reducing until it reaches zero at the end. The adjoint variables function satisfies the transversal criteria necessary in the optimal control problem, as shown in Figure 9. Furthermore, the window period stage of HIV is a narrow stage that might open a gate for HIV transmission in the population without effective preventative control efforts, but the other stages of HIV development can be controlled with good preventive and treatment control interventions.

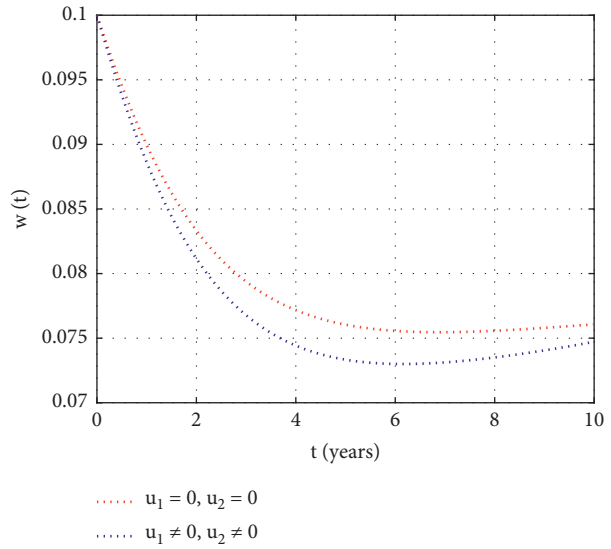

Figure 5: Simulation of window population size without and with controls.

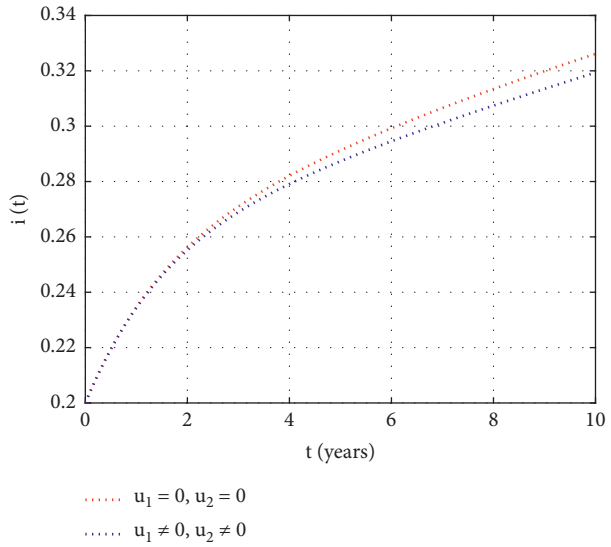

Figure 6: Simulation of HIV population size without and with controls.

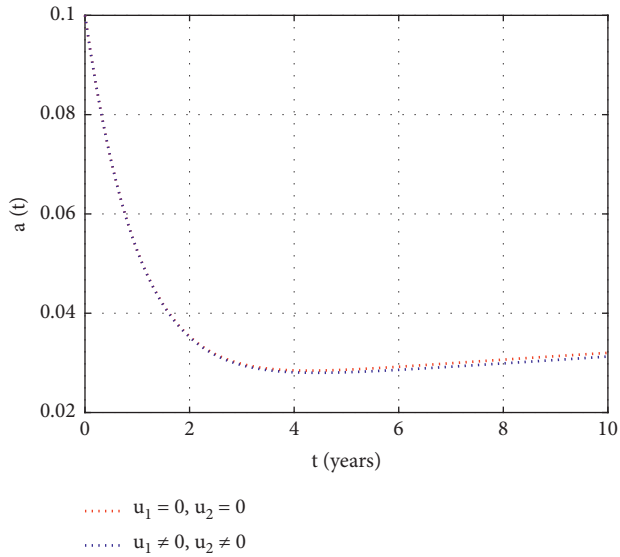

Figure 7: Simulation of AIDS population size without and with controls.

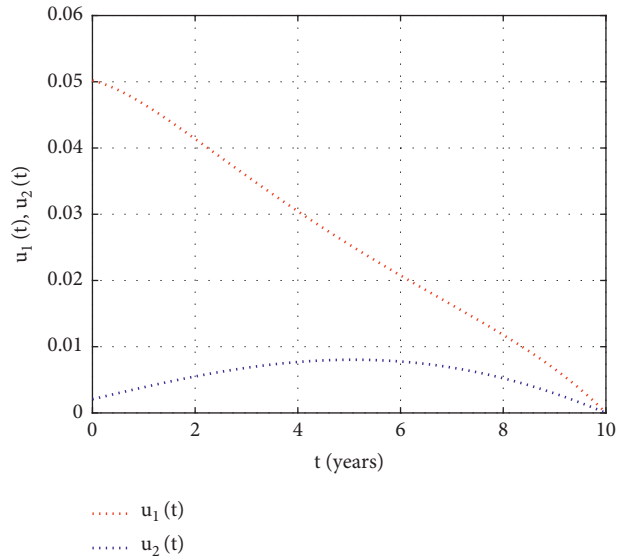

Figure 8: Simulation of preventive and treatment controls.

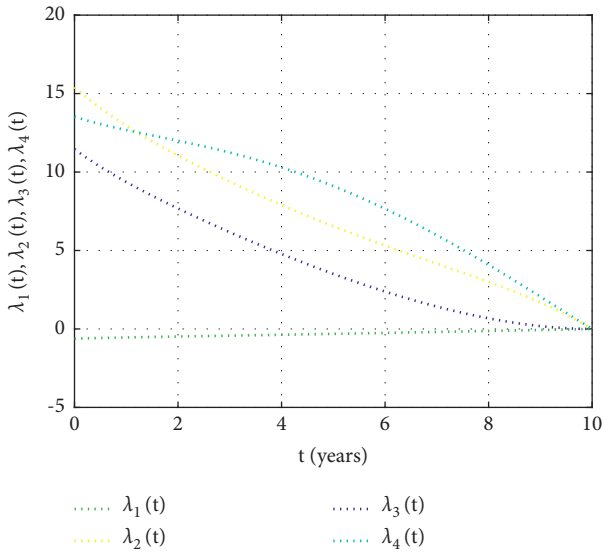

FIGURE 9: Simulation of susceptible population size without and with controls.

7. Conclusion

In this study, a new method is applied to determine a kind of bifurcation at $R_0 = 1$, and the stability analysis is carried out if $R_0 < 1$ and $R_0 > 1$. The current study finding shows that the endemic equilibrium of model (4) exhibits forward bifurcation at $R_0 = 1$. The transmission of HIV persists in the population if $R_0 > 1$ and extincts if $R_0 < 1$. According to the findings of the sensitivity analysis, an increase in the rate of HIV transmission from HIV persons contributes to the prevalence of HIV in the community. When both preventative and treatment control strategies are employed combined, they are more effective in limiting the transmission dynamics of the human immunodeficiency virus. Moreover, the cost-effectiveness analysis shows that the control measures are more economically consumed if both controls are applied together in controlling the human immunodeficiency virus.

Data Availability

No data were used in this manuscript.

Disclosure

This study is a part of a Wollega University Ph.D. thesis.

Conflicts of Interest

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

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