Abstract

Prophylaxis (PrEP) is considered one of the promising interventions against HIV infection as trials on various groups and sites have reported its significant effectiveness. From the studies done, analysis of the data collected shows that PrEP has the potential to help prevent HIV infections and slow the HIV epidemic. In this paper, a deterministic model that incorporates PrEP is developed to assess the impact of the use of PrEP on the transmission of HIV/AIDS. Stability analysis of the model showed that DFE is locally and globally asymptotically stable when $R_p < 1$. The EE exists and is locally and globally asymptotically stable when $R_p > 1$. PrEP effectiveness is achieved if taken effectively, hence lack of adherence to PrEP substantially increases the risk of HIV infection among the high risk individuals.

Keywords: HIV/AIDS, PrEP, Sensitivity Analysis

1 Introduction

Treatment of HIV/AIDS infection has improved dramatically in the past few decades but is still limited by the development of drug resistance and the inability of current therapies to completely eradicate the virus from an individual. The World Health Organization’s (WHO) Global Health Sector Strategy on
HIV embraces innovation in the HIV treatment, prescribing, for example, that people at substantial risk of HIV infection should be offered pre-exposure prophylaxis (PrEP) as an additional prevention strategy [12]. Thus, a HIV/AIDS model that incorporates the use of PrEP and study its long term solutions is developed in this paper.

2 Model Formulation

Pre-exposure prophylaxis (PrEP) is a HIV prevention strategy whereby uninfected hosts take drugs that are similar to (or the same as) ART in order to reduce their susceptibility to infection [12]. PrEP resembles anti-infection vaccines [2], however, PrEP differs from traditional anti-infection vaccines in an important way: if a host on PrEP becomes infected, the viruses they harbour will immediately be exposed to anti-retroviral drugs resulting in viral clearance. The dynamics of the model is described schematically in Figure 1:

\[
\dot{S}(t) = \Lambda - \mu S(t) - \omega S(t) - \frac{\beta CI(t)S(t)}{N(t)},
\]

Figure 1: A Flow Diagram of a HIV/AIDS Model Incorporating Prophylaxis Use

The corresponding mathematical equations of the schematic diagram can be described by a system of ordinary differential equations;
\[ \dot{P}(t) = \omega S(t) - \mu P(t) - \frac{(1 - \eta)\beta C I(t) P(t)}{N(t)}, \]
\[ \dot{I}(t) = \frac{\beta C I(t) S(t)}{N(t)} + \frac{(1 - \eta)\beta C I(t) P(t)}{N(t)} - (\nu + \theta + \mu) I(t), \]
\[ \dot{T}(t) = \delta A(t) + \theta I(t) - (\gamma + \mu) T(t), \]
\[ \dot{A}(t) = \gamma T(t) + \nu I(t) - (d + \mu + \delta) A(t), \]

(1)

where; \( \Lambda \) recruitment rate of the susceptibles, \( \mu \) is the natural mortality rate, \( \beta \) represents the contact rate with HIV, \( C \) is the average number of sexual partners, \( \omega \) represents the PrEP uptake rate, \( \eta \) is the PrEP efficacy, \( \nu \) represents the rate of progression of HIV infectives to Aids, \( \theta \) is the ART uptake rate amongst the infected individuals, \( \gamma \) is the rate of progression to AIDS class due to resistance to treatment (drug resistance), \( \delta \) is the rate at which Aids patients get treatment, and finally \( d \) is the disease induced death rate in the Aids patients class.

Since the model in Equation (1) describes a human population, the model developed is positive and bounded for all \( t \geq 0 \) with;

\[ N(t) = S(t) + P(t) + I(t) + T(t) + A(t). \]

Thus all the state variables in Equation (1) will remain positive so that the solutions of the model with positive initial conditions will remain positive for all \( t > 0 \). Using the next generation matrix approach [4], the next generation matrix of model (1)

\[ R_p = \frac{\beta C}{(\nu + \theta + \mu)} \left( \frac{\mu + \omega(1 - \eta)}{\mu + \omega} \right), \]

(2)

3 Local Stability Analysis of the Disease Free Equilibrium

The model developed in Equation (1) has a disease free equilibrium (DFE) given by

\[ \Sigma_0 = (S(0), P(0), I(0), T(0), A(0)) = \left( \frac{\Lambda}{\mu + \omega}, \frac{\omega \Lambda}{\mu(\mu + \omega)}, 0, 0, 0 \right) \]

(3)

Theorem 1. If \( R_p < 1 \), then \( E_0 = \left( \frac{\Lambda}{\mu + \omega}, \frac{\omega \Lambda}{\mu(\mu + \omega)}, 0, 0, 0 \right) \) is the equilibrium in \( \Gamma_0 \) and is locally asymptotically stable.
Proof. Evaluating the Jacobi matrix of Equation (1) at DFE we have

$$J(E_0) = \begin{pmatrix}
-\mu - \omega & 0 & -\beta C & 0 & 0 \\
\omega & -\mu & 0 & 0 & 0 \\
0 & 0 & (\theta N(t) + \frac{\beta CS(t)}{N(t)}) - (\nu + \theta + \mu) & 0 & 0 \\
0 & 0 & \theta & -\gamma & -\delta \\
0 & 0 & \nu & \gamma & -(d + \mu + \delta)
\end{pmatrix}$$

(4)

To investigate the stability of the DFE, we compute the eigenvalues of Equation (4).

$$\begin{vmatrix}
-\mu - \omega - \lambda & 0 & -\beta C & 0 & 0 \\
\omega & -\mu - \lambda & -(1 - \eta)\beta C & 0 & 0 \\
0 & 0 & (\nu + \theta + \mu)[R_p - 1] - \lambda & 0 & 0 \\
0 & 0 & \theta & -\gamma - \lambda & \delta \\
0 & 0 & \nu & \gamma & -(d + \mu + \delta) - \lambda
\end{vmatrix} = 0$$

(5)

Using the Routh Hurwitz criterion [6], the eigenvalues obtained by the matrix (5) are negative since the trace=$\gamma + 4\mu + d + \delta + \omega + (\nu + \theta + \mu)[R_p - 1] < 0$ and determinant=$-(\nu + \theta + \mu)[R_p - 1]\mu(\mu + \omega)[\gamma(d + \mu) + \mu(d + \mu + \delta)] > 0$ when $R_p < 1$. Hence, the endemic equilibrium $E^*$ is locally asymptotically stable whenever $R_p < 1$.

Given a small infective population, each infected individual in the entire period of infectivity will produce on average less than one infected individual when $R_p < 1$. This shows that the disease is eliminated in the population when $R_p < 1$.

4 Global Stability Analysis of the Disease Free Equilibrium

In this section the Global asymptotic stability of the disease free equilibrium is analyzed using the theorem by Castillo Chavez et. al. [1].

Theorem 2. The fixed points $E_0 = (X^*, 0)$ is Globally asymptotically stable provided $R_p < 1$.

Proof. Consider

$$F(X, 0) = (\Lambda - (\mu + \omega)S(t), \omega S(t) - \mu P(t))$$
\begin{align*}
G(X, Z) &= AZ - \hat{G}(X, Z) \\
\text{where}
A &= \begin{pmatrix}
-(\nu + \theta + \mu) & 0 & 0 \\
\theta & - (\gamma + \mu) & \delta \\
\nu & \gamma & -(d + \mu + \delta)
\end{pmatrix}
\end{align*}

and
\[\hat{G}(X(t), Z(t)) = \begin{pmatrix}
\hat{G}_1(X(t), Z(t)) \\
\hat{G}_2(X(t), Z(t)) \\
\hat{G}_3(X(t), Z(t))
\end{pmatrix} = \begin{pmatrix}
\beta C \left(1 - \frac{S(t) + \eta P(t)}{N}\right) I(t) \\
0 \\
0
\end{pmatrix} \]

It follows that \(\hat{G}_1(X(t), Z(t)) \geq 0, \hat{G}_2(X(t), Z(t)) = \hat{G}_3(X(t), Z(t)) = 0\) thus \(\hat{G}(X(t), Z(t)) \geq 0\). Conditions \(M_1\) and \(M_2\) are satisfied and thus \(E_0\) is Globally Asymptotically Stable for \(R_p < 1\).

Global asymptotic stability shows that regardless of any starting solution, the solutions of the model will converge to DFE whenever \(R_p < 1\).

### 5 Local Stability Analysis of the Endemic Equilibrium

The endemic equilibrium state is the state where the disease cannot be totally eradicated but remains in the population at manageable levels. HIV/AIDS is endemic or persistent in the population if \(S^*(t), I^*(t), T^*(t), A^*(t) > 0\) for all \(t > 0\). To investigate the stability the endemic equilibrium of model (1), linearization of model (1) at Endemic equilibria is done. The Jacobian of model (1) at \(E^* = (S^*, P^*, I^*, T^*, A^*)\) is:

\[
J = \begin{pmatrix}
-\mu - \omega - \frac{\beta CI^*}{N} & 0 & 0 & 0 & 0 \\
\omega & -\mu - \frac{(1-\eta)\beta CI^*}{N} & -\frac{\beta CS}{N} & 0 & 0 \\
\frac{\beta CI^*}{N} & \frac{(1-\eta)\beta CI^*}{N} & a_1 & 0 & 0 \\
0 & 0 & \theta & -(\gamma + \mu) & \delta \\
0 & 0 & \nu & \gamma & -(d + \mu + \delta)
\end{pmatrix}
\]

where \(a_1 = \frac{\beta CS^*}{N} + \frac{(1-\eta)\beta CP^*}{N} - (\nu + \theta + \mu)\). For stability of system (6), we compute its eigenvalues which involves the solution of the system:

\[
\begin{vmatrix}
-\mu - \omega - \frac{\beta CI^*}{N} - \lambda & 0 & 0 & 0 & 0 \\
\omega & -\mu - \frac{(1-\eta)\beta CI^*}{N} - \lambda & -\frac{\beta CS}{N} - \lambda & 0 & 0 \\
\frac{\beta CI^*}{N} & \frac{(1-\eta)\beta CI^*}{N} & a_1 - \lambda & 0 & 0 \\
0 & 0 & \theta & -(\gamma + \mu) - \lambda & \delta \\
0 & 0 & \nu & \gamma & -(d + \mu + \delta) - \lambda
\end{vmatrix} = 0
\]
The characteristic equation of (7) is given by:

$$P(\lambda) = \lambda^5 + A\lambda^4 + B\lambda^3 + D\lambda^2 + E\lambda + G = 0 \quad (8)$$

where

$$A = 4\mu + \omega + 2(1 - \eta)\frac{\beta CI^*}{N} + \gamma + d + \delta + \frac{\beta CI^*}{N}$$

$$B = \left(\mu + \omega + \frac{\beta CI^*}{N}\right)\left(2\mu + \delta + d + (1 - \eta)\frac{\beta CI^*}{N}\right) + \frac{\beta^2 C^2 S^* I^*}{N^2} + (1 - \eta)^2 \frac{\beta^2 C^2 I^* P^*}{N^2}$$

$$+ \mu(d + \mu + \delta) + (\gamma + \mu)(\mu + \omega + \frac{\beta I^*}{N} + (\gamma + \mu)\left[(R_p - 1)(\nu + \theta + \mu) + \mu + (1 - \eta)\frac{\beta CI^*}{N}\right]$$

$$- (d + \mu + \delta)\left[\left(\mu + \omega + \frac{\beta CI^*}{N}\right)(\nu \gamma + \nu \mu)\frac{\beta CI^*}{N}\right]$$

$$D = \frac{\beta^2 C^2 S^* I^*}{N^2} \left[3\mu + (1 - \eta)\frac{\beta CI^*}{N} + d + \delta + \gamma\right] + \left(\mu + \omega + \frac{\beta CI^*}{N}\right)\left(1 - \eta\right)\omega \frac{\beta CI^*}{N}$$

$$+ \delta \theta \left(\mu + \omega + \frac{\beta CI^*}{N}\right) + \left(\mu + \omega + \frac{\beta CI^*}{N}\right)(\nu + \theta + \mu)(R_p - 1) - \theta \omega (1 - \eta)\frac{\beta CI^*}{N}$$

$$E = \left[\frac{\beta^2 C^2 S^* I^*}{N^2} \left(\mu + (1 - \eta)\frac{\beta CI^*}{N}\right) + \left(\mu + \omega + \frac{\beta CI^*}{N}\right)(\mu + \nu + \theta)(R_p - 1)\right](d + \mu + \delta)$$

$$+ \left[\left(\mu + \omega + \frac{\beta CI^*}{N}\right)\left(\mu + (1 - \eta)\frac{\beta CI^*}{N}\right) + (1 - \eta)^2 \frac{\beta^2 C^2 P^* I^*}{N^2}\right](\gamma + \mu)$$

$$+ \mu(d + \mu + \delta)\left[\beta C S^* \omega(1 - \eta)\frac{\beta CI^*}{N} + \left(\mu + \omega + \frac{\beta CI^*}{N}\right) + \frac{\beta^2 C^2 S^* I^*}{N^2}\right]$$

$$G = \left[\frac{\beta^2 C^2 S^* I^*}{N^2} \left(\gamma + \mu\right)(d + \mu + \delta) + d \gamma \mu + \omega d \gamma + \beta d \gamma\right]\left(\mu + (1 - \eta)\frac{\beta CI^*}{N}\right)(\gamma + 2\mu + d + \delta)$$

$$+ \left[\frac{\beta^2 C S^*}{N^2} (1 - \eta) + (\mu + \omega + \frac{\beta CI^*}{N})\left[(\nu + \theta + \mu)(R_p - 1) + \mu + (1 - \eta)\frac{\beta CI^*}{N}\right]\right]$$

Thus, the number of possible negative real roots of equation (9) depends on the signs of $A, B, D, E, \& G$. This can be analyzed using the Descartes Rules of Signs of the polynomial given by [13]:

$$P(\lambda) = A\lambda^4 + B\lambda^3 + D\lambda^2 + E\lambda + G \quad (9)$$

From Descartes Rule of Signs [13], the number of negative real zeros of $P$ is either equal to the number of variations in sign of $P(-\lambda)$ or less than this by an even number. Thus, the possibilities of negative roots of Equation (9) is as summarized in Table 1.
Table 1: Roots of the Characteristic Equation

<table>
<thead>
<tr>
<th>Cases</th>
<th>A</th>
<th>B</th>
<th>D</th>
<th>E</th>
<th>G</th>
<th>$R_p &gt; 1$</th>
<th>No. of Sign Changes</th>
<th>No. of - roots</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>4</td>
<td>4,2</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>$R_p &gt; 1$</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

From Table 4.1, the maximum number of variations of signs in $P(-\lambda)$ is four, hence the characteristic polynomial (9) has four negative roots. Thus,

$$P(-\lambda) = -\lambda^5 + A\lambda^4 - B\lambda^3 + D\lambda^2 - E\lambda + G = 0$$  \hspace{1cm} (10)

has negative roots. Therefore, whenever $1 - \eta > 0$ and if cases 1-8 in Table 1 are satisfied, model (1) is locally asymptotically stable if $R_p > 1$.

Epidemiologically, given a small infective population, each infected individual in the entire period of infectivity will produce on average less than one infected individual when $R_p > 1$. This shows that persistence of the infection occurs whenever $R_p > 1$.

6 Global Stability Analysis of the Endemic Equilibrium

Consider the following Lyapunov function;

$$V = S - S^* \ln S + P - P^* \ln P + I - I^* \ln I + T - T^* \ln T + A - A^* \ln A$$  \hspace{1cm} (11)

Differentiating $V$ with respect to time gives

$$\dot{V} = \left(1 - \frac{S^*}{S}\right) \dot{S} + \left(1 - \frac{P^*}{P}\right) \dot{P} + \left(1 - \frac{I^*}{I}\right) \dot{I} + \left(1 - \frac{T^*}{T}\right) \dot{T} + \left(1 - \frac{A^*}{A}\right) \dot{A}$$  \hspace{1cm} (12)

Replacing $\dot{S}, \dot{P}, \dot{I}, \dot{T}, \dot{A}$ from Equation (1) in (12), we obtain;

$$\dot{V} = \left(1 - \frac{S^*}{S}\right) [\Lambda - \mu S - \omega S - \frac{\beta CI S}{N}] + \left(1 - \frac{I^*}{I}\right) \left[\frac{\beta CI S}{N} + \frac{(1 - \eta)\beta CIP}{N} - (\nu + \theta + \mu)I\right]$$
\[
\begin{align*}
+ \left(1 - \frac{P^*}{P}\right) \left[\omega S - \mu P - (1-\eta)\frac{\beta CIP}{N}\right] + \left(1 - \frac{T^*}{T}\right) \left[\delta A + \theta I - (\gamma + \mu)T\right] \\
+ \left(1 - \frac{A^*}{A}\right) \left[\gamma T + \nu I - (d + \mu + \delta)A\right]
\end{align*}
\]

(13)

At the boundary \(N \leq \frac{\Lambda}{\mu}\), thus we let \(N = \frac{\Lambda}{\mu}\) and using the following relations at the steady state,

\[
\begin{align*}
\Lambda &= \mu S^* + \omega S^* + \frac{\beta \mu C I^* S^*}{\Lambda}, \quad \gamma T^* + \nu I^* = (d + \mu + \delta)A^*, \\
\frac{\mu \beta CS^*}{\Lambda} + \frac{\mu \beta CP^*}{\Lambda} &= (\nu + \theta + \mu), \quad \delta A^* + \theta I^* = (\gamma + \mu)T^* \\
\mu P^* &= \omega S^* - \eta \frac{\beta \mu C I^* P^*}{\Lambda}
\end{align*}
\]

and after simplifications, Equation (14) becomes

\[
\begin{align*}
\dot{V} &= \left(1 - \frac{S^*}{S}\right) \left[\mu S^* + \omega S^* + \frac{\beta \mu C I^* S^*}{\Lambda} - \mu S - \omega S - \frac{\beta \mu C I S}{\Lambda}\right] \\
&+ \left(1 - \frac{I^*}{I}\right) \left[\frac{\beta C I S \mu}{\Lambda} + \frac{\eta \beta C I P \mu}{\Lambda} - (\nu + \theta + \mu)I\right] + \left(1 - \frac{P^*}{P}\right) \left[\omega S - \mu P - (1-\eta)\frac{\beta C I P \mu}{\Lambda}\right] \\
&+ \left(1 - \frac{T^*}{T}\right) \left[\delta A + \theta I - (\gamma + \mu)T\right] + \left(1 - \frac{A^*}{A}\right) \left[\gamma T + \nu I - (d + \mu + \delta)A\right] \\
&= \left(\frac{\beta \mu C I^* S^*}{\Lambda} + \mu S^* + \omega S^*\right) \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \omega S^* \left(1 - \frac{S^*}{S}\right) + \frac{\beta \mu C I S}{\Lambda} \left(1 - \frac{S}{S^*}\right) \\
&+ \frac{(1-\eta)\beta \mu C P^* I}{\Lambda} \left(1 - \frac{P^*}{P}\right) + \gamma T^* \left(1 - \frac{A^* T}{A^* T^*}\right) + \nu I^* \left(1 - \frac{A^* I}{A I^*}\right) \\
&+ \delta A^* \left(1 - \frac{T^* A}{T A^*}\right) + \theta I^* \left(1 - \frac{T^* A}{T A^*}\right)
\end{align*}
\]

(14)

From the property that the geometric mean is less than or equal to the arithmetic mean, the inequality \(\frac{dV}{dt} = 0\) holds iff \((S = S^*, P = P^*, I = I^*, T = T^*, A = A^*)\). By Lassalles’s invariance principle [3], every solution of the system (1) with initial conditions in \(\{(S, P, I, T, A) \in \mathbb{R}^5 : N \leq \frac{\Lambda}{\mu}\}\) approaches the endemic equilibrium, thus the endemic equilibrium \(E^*\) is Globally Asymptotically stable. Epidemiologically, this implies that any perturbation of the model by introduction of infectives into the population makes the model to converge to the endemic equilibrium \(E^*\).

7 Conclusion

Pre-exposure prophylaxis (PrEP) is considered one of the promising interventions against HIV/AIDS infection as experiments on various groups and
sites have reported its significant effectiveness [4]. Despite the advocacy of behavior change and scale-up of ART therapy, new incident infections continues to be a problem. Thus, the importance of combination of prevention approaches to the transmission of HOV/AIDS. From the results, if the reproduction number $R_p$ is less than unity then the DFE is locally and globally asymptotically stable, while if $R_p > 1$, the endemic equilibrium is asymptotically stable. This shows that use of PrEP will lower the HIV/AIDS prevalence if used effectively.

References


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