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A SIR Epidemic Model for HIV/AIDS Infection

G.C.E Mbah, D. Omale, B. O. Adejo,

Abstract - In this article, we survey the stability analysis and the basic reproduction number (R_0) that are significant concepts for the development of HIV/AIDS mathematical models. Furthermore, we developed a model to confirm the endemicity of the disease by using the basic reproduction number R_0 as a basis.

Keywords Terms - Reproduction, Epidemiology, HIV, Mathematical Modeling, Virus, Model

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1. INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system of human beings and renders it weak to infection. HIV can progress to Acquired Immune Deficiency Syndrome (AIDS) once the number of T-cells in the immune system have been significantly reduced (UNAIDS 2007). During the initial infection, a person may experience a brief period of influenza like illness. This is usually followed by a prolonged period without symptoms. As the illness progresses, it interferes more and more with the immune system thereby making the person much more likely to get infections such as opportunistic infections and tumor that do not usually affect people who have working immune systems.

HIV infects vital cells in the human immune system such as the helper T cells specially $CD_4^+\ T\ cells,$ macrophages and dendritic cell (Cunningham A. Dinagby et al (2010)). HIV infection leads to low level of $CD_4^+\ T\ cells$ through a number of mechanisms includes apoptosis of uninfected cells by stander cells direct viral killing of infected cells, and killing of infected $CD_4^+\ T\ cells$ by $CD8\ T-cells$ cytotoxic limphocytes that recognizes infected cells. Garg H. Mhl. J. Joshi A. (2012), Kumar V (2012) leading to decline of $CD_4^+\ T-cells$ beyond a critical level which will lead to a lose of cell mediated immunity and the body becomes progressively more susceptible to opportunistic infections.

HIV is transmitted primarily via unprotected sexual intercourse which may include anal or even oral sex, contaminated blood transfusions, hypodemic needles and from mother to child transmission during pregnancies delivery or breast feeding. (William N. R and Steven B. (2007)). Some bodily fluids such as saliva and tears do not transmit HIV (CDC (2003)). Prevention is primarily through safe sex and needle exchange program is a key strategy to control the spread of the disease. There is no known cure or vaccines for AIDS for now, however HAART can reduce or slow the course of the disease and may lead to normal life expectancy. Since it was first recognized in 1981 by Centre for Disease Control and Prevention (CDC), AIDS has caused over 34 million deaths as of 2010 (CDC (2011)). As of 2010, approximately 36 million people are living with HIV/AIDS globally (UNAID (2010)). AIDS is now a global pandemic in the 21st century.

Numerous deterministic and stochastic models since mid 1980s have been developed to describe the immune system and its interaction with HIV. Stochastic models aims to account for the early events in the disease when there are few infected cells and small number of virus. Nowak et al (1996) investigated the effects of variability among vital strains, this and other works have been commented on critically by Stillianakis, N. I. et al (1994).

Most models appearing in literature have been deterministic in nature, such as Mclean and Nowak (1992), Frost and Mclean (1994), Kirschner and Webb (1997) and Wein et al (1998) models. These models try to reflect the dynamical change in mean cell populations. These models typically consider the dynamics of the $CD4$ cells. Latertly inflected cells and virus population, as well as effects of drug therapy.

In this article, we develop and analyze a SIR model to study the dynamics of HIV/AIDS infections within the human immune system by the considering the stability and the basics reproduction number. The immune system is a collection of cells and organs that work together synergistically. The T-cells are the subsets of white blood cells, which includes the $CD_4^+\ T\ cells$ (helper cells that signal when invaders enter) $CD8\ T-cells$ (killer T-cells, which produce antibodies to kill invaders). The virus HIV target the $CD_4^+\ T\ cells$ not to send strong signal for the $CD8\ T-cells$ to produce the antibodies. This cause immunodeficiency (stage of AIDS).

2. MODEL FORMULATION

We assume that the population are homogeneously mixed and the interaction within the population is a mass action type, cells once infected start producing virus. Furthermore, we ignore the latency period and there is a constant migration of susceptible into the population of size N (t) infected cells which produces same number of virus particles.

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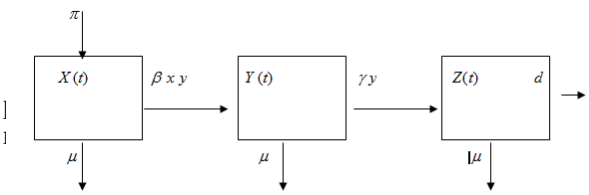
Let $x(t)$, $y(t)$ and $z(t)$ denote the number of susceptible, infectious and those that have developed acute AIDS (i.e AIDS patient).

We assume a natural death throughout the population at the rate μ.

The schematic diagram of the disease on which we base our model is as follows:



$$y' = \beta\, x\, y - \gamma y - \mu y \qquad \ldots (2.2)$$
$$z' = \gamma y - \mu z - dz \qquad \ldots (2.3)$$

π = Recruitment of susceptible into the population

μ = Natural death rate

d = Death rate of infected cells which also includes the possibility of death by busting of the cell, hence $d \geq \mu$

β = Rate at which susceptible becomes infected with the virus

γ = The rate at which infectious moves to full blown AIDS

The total population at time t is given by
$N(t) = x(t) + y(t) + z(t)$. Thus,

$$\frac{dn}{dt} = (\pi - \mu)\, N - dz$$

We note that in the absence of the disease and infectious, the total population size N is stationary for $\pi = \mu$; decline for $\pi < \mu$ and grows exponentially for $\pi > \mu$. So we shall assume a mortality rate μ that will be a function of state variable. Since the model is homogeneous of degree one, the variable can be normalized.

Thus $x = X$, $y = Y$, $z = Z$, this leads to a normalized system;

$$(Z, Y, Z) = (x, y, z)$$

$$\pi - \beta xy - \mu x = 0 \qquad \ldots . (2.4)$$

$$\beta xy - (\gamma + \mu) y = 0 \qquad \ldots . (2.5)$$

$$\gamma y - (\mu + d) z = 0) \qquad \ldots . (2.6)$$

where $x + y + z = 1$ and
$x(t) > 0,\ y(0) > 0\ \ z(0) > 0\ \forall\ t \geq 0$

The continuity of equation (2.4) – (2.6) indicate that the model is well possed for $N > 0$.

3. MODEL ANALYSIS

3.1 Existence of disease - free equilibrium state E_1.

At the disease free equilibrium state, we have absence of infection. Thus, all the infected classes will be zero and the entire population will comprises of only susceptible individuals.

Theorem 1: A disease free equilibrium state of the model exist at the point.

$$(x^*, y^*, z') = \left(\pi/\mu, 0, 0\right).$$

Proof: At equilibrium, the rate of change of each variable is equal to zero.

i. e $\dfrac{dx^0}{dt} = \dfrac{dy^0}{dt} = \dfrac{dz^0}{dt} = 0 \qquad \ldots . (3.1)$

from equation (2.5)

$$y^*[\beta x - (\gamma + \mu)] = 0 \qquad \ldots . (3.2)$$
$$\Rightarrow y^* = 0 \text{ or} \qquad \ldots . (3.3)$$
$$\beta x^* - (\gamma + \mu) = 0 \qquad \ldots . (3.4)$$

Substitute (3.3) in (2.6)

$$\Rightarrow z^* = 0 \qquad \ldots . (3.5)$$

Substitute (3.3) and (3.5) into (2.6)

$$\pi - \beta x^* y^* - \mu x^* = 0$$
$$\Rightarrow \pi - \mu(x) = 0$$
$$x^* = \pi/\mu \qquad \ldots . (3.6)$$
$$\Rightarrow x^* = \pi/\mu,\ y^* = 0,\ z^* = 0$$
$$(x^\infty, y^\infty, z^\infty) = \left(\pi/\mu, 0, 0\right)$$

Hence the disease free-equilibrium state exist.

3.2 Existence of Endemic Disease Equilibrium State

At the endemic equilibrium state the disease is present. Therefore the susceptible, infectious and the removed classes are not anyway equal to zero.

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Theorem II: An endemic equilibrium state of the model exist at the points

$$(x,\ y\ z) = \frac{\gamma+\mu}{\beta}, \frac{\mu\gamma+\mu^2+\pi\beta}{\beta(\gamma+\mu)}, \frac{\mu\gamma+\mu^2+\pi\beta}{\beta(\gamma+\mu)(\mu+\delta)}.$$

Proof: Since at the equilibrium state of the endemic case, the disease is present, then;

$$\frac{ds^*}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = (x_0,\ y_0,\ z_0)$$

From equations (2.1), (2.2) and (2.3) we have,

$$\pi - \beta xy - \mu x = 0 \quad \ldots. (3.7)$$

$$\beta xy - (\gamma+\mu)y = 0 \quad \ldots. (3.8)$$

$$\gamma y - (\mu+\delta)z = 0 \quad \ldots. (3.9)$$

From (3.9)

$$\gamma y - (\mu+\delta)z = 0$$

$$\Rightarrow \gamma y = (\mu+\delta)z$$

$$y = \left(\frac{\mu+\delta}{\gamma}\right)z \quad \ldots. (3.10)$$

Substituting (3.10) in (3.7) we have

$$\pi - \frac{\beta(\mu+\delta)}{\gamma} zx - \mu x = 0 \quad \ldots. (3.11)$$

Substituting (3.10) in (3.8)

$$\Rightarrow \beta x - (\gamma+\mu)\left(\frac{\mu+\delta}{\gamma}\right)z = 0 \quad \ldots. (3.12)$$

From (3.12)

$$\beta\mu zx - (\gamma+\mu)\,\mu z + \beta x\delta z - (\gamma+\mu)\,\delta z = 0$$

$$(\beta\mu+\beta\delta)\,zx - (\gamma\mu+\gamma\delta+\mu\delta+\mu^2)z = 0$$

$$\Rightarrow z[\beta(\mu+\delta)\,x - (\mu+\delta)(\mu+\gamma)] = 0$$

$$\Rightarrow z = 0 \ \ or$$

$$\beta(\mu+\delta)x - (\mu+\delta)(\mu+\gamma) = 0$$

$$\Rightarrow x = \frac{(\mu+\delta)(\mu+\gamma)}{\beta(\mu+\delta)}$$

$$\Rightarrow x = \frac{\mu+\gamma}{\beta} \quad \ldots (3.13)$$

Substituting (3.13) in (3.7)

$$\pi - (\beta y+\mu)\left(\frac{\mu+\gamma}{\beta}\right) = 0$$

$$\Rightarrow \pi\beta - ((\beta\mu+\beta\gamma)\,y + \mu\gamma+\mu^2) = 0$$

$$\Rightarrow (\beta\mu+\beta\gamma)\,y = \mu\gamma+\mu^2-\pi\beta$$

$$y = \frac{\pi\beta-\mu\gamma-\mu^2}{\beta(\gamma+\mu)} \quad \ldots. (3.14)$$

From equation (3.10)

$$z = \frac{\gamma y}{\mu+\delta} \quad \ldots. (3.15)$$

Substituting from (3.14)

$$\frac{z = \gamma\left(\frac{\pi\beta-\mu\gamma-\mu^2}{\beta(\gamma+\mu)}\right)\gamma}{\mu+\delta}$$

$$\Rightarrow z = \frac{\pi\beta-\mu\gamma-\mu^2}{\beta(\gamma+\mu)(\mu+\delta)} \quad \ldots. (3.16)$$

Therefore at the endemic state, we have

$$\left.\begin{aligned} x &= \frac{\gamma+\mu}{\beta} \\ y &= \frac{\mu\gamma+\mu^2+\pi\beta}{\beta(\gamma+\mu)} \\ z &= \frac{\mu\gamma+\mu^2+\pi\beta}{\beta(\gamma+\mu)(\mu+\delta)} \end{aligned}\right\} \quad \ldots. (3.17)$$

which indicates that the disease is endemic in the population, the susceptible, infection and the removed cases are seriously affected.

3. Effective Basic Reproduction Number R_0

The basic reproduction number represent the average number of secondary cases generated by an infected individual if introduced into the susceptible population with no immunity to the disease in the absence of intervention to control the infections.

If R_0 is less than 1, the infected individual produces less than are newly infected individual over the course of the infection period, therefore the disease will dies out at along run. Conversely if $R_0 > 1$ each infected individual produces an average more than one new infection, the infection will be

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able to spread in a population. A large value of R_0 indicate that the disease can turn to an epidemic case over long run. Heesterbeek and Dietz (1996) using the technique introduced by Dickman and Heesterbeek (2000) and subsequently proofed by Vanden and Watmough (2005). We obtained the basic reproduction number R_0 of the our models which is the spectral radius (ℓ) of the next generation matrix K.

$$R_0 = \ell\, k$$

where $k = FV^{-1}$

$$R_0 = \ell\left(Fv^{-1}\right)$$

$$F = \begin{pmatrix} \beta_x & 0 \\ 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} 0 & 0 \\ \gamma & 0 \end{pmatrix}$$

$$V^{-1} = \begin{pmatrix} k & 0 \\ 0 & k_2 \end{pmatrix}$$

based on the equations in the SIR model analyzed above

$$V = V^- - \cup^+$$

$$V = \begin{pmatrix} k & 0 \\ \gamma & k_2 \end{pmatrix}$$

$$V^{-1} = \frac{1}{k_1 k_2}\begin{bmatrix} k_2 & 0 \\ \gamma & k_1 \end{bmatrix}$$

$$= \begin{bmatrix} \frac{1}{k_1} & 0 \\ \frac{\gamma}{k_1 k_2} & \frac{1}{k_2} \end{bmatrix} \quad \ldots. (3.18)$$

$$FV^{-1} = \begin{bmatrix} \beta_x & 0 \\ 0 & 0 \end{bmatrix}\begin{bmatrix} \frac{1}{k_1} & 0 \\ \frac{\gamma}{k_1 k_2} & \frac{1}{k_2} \end{bmatrix}$$

$$= \begin{bmatrix} \frac{\beta x}{k_1} & 0 \\ 0 & 0 \end{bmatrix}$$

$$\ldots. (3.19)$$

We now seek for the highest dominant eigen values

$$\ell\left(Fv^{-1}\right) = \begin{bmatrix} \frac{\beta x}{k} & 0 \\ 0 & -\lambda \end{bmatrix} \quad \ldots. (3.20)$$

$$\Rightarrow \left(\frac{\beta x}{k} - \lambda\right)(\lambda) = 0$$

$$\Rightarrow \lambda = 0 \quad \ldots. (3.21)$$

or $\lambda = \frac{\beta x}{k}$ $\quad \ldots. (3.22)$

since the value of $x = \pi/\mu$, this implies that

$$\frac{\beta\pi}{\mu k_1} = R_0$$

$$\ldots. (3.23)$$

R_0 is the basic reproduction number

4. Local Stability of Disease Free Equilibrium (DFE) State

From equation (3.7), (3.8) and (3.9), we have the Jacobian matrix

$$\begin{pmatrix} \beta y - \mu & -\beta x & 0 \\ \beta y & \beta x - (\gamma + \mu) & 0 \\ 0 & \gamma & \mu + \delta \end{pmatrix} .(3.24)$$

For local stability of DFE state, we have $(x^*,\ y^*,\ z^*) = (\mu, 0, 0) = \left(\pi/\mu, 0, 0\right)$ linearization of the equation, gives the Jacobian matrix

$$J(E_x) = \begin{bmatrix} -\mu & \frac{\beta\pi}{\mu}, & 0 \\ 0 & \frac{\beta\pi}{\mu} - (\gamma + \mu) & 0 \\ 0 & \gamma & -(\mu + \delta) \end{bmatrix} \ldots (3.25)$$

we set $\gamma + \mu = k_1$ and $\mu + \delta = k_2$ without loss of generality we have

$$J(E_x) = \begin{bmatrix} -\mu & \frac{-\beta\pi}{\mu} & 0 \\ 0 & \frac{\beta\pi}{\mu} - k_1 & 0 \\ 0 & \gamma & -k_2 \end{bmatrix} (3.26)$$

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$$= \begin{vmatrix} -\mu-\lambda_1 & \frac{-\beta\pi}{\mu} & 0 \\ 0 & \frac{\beta\pi}{\mu}-k_1-\lambda_2 & 0 \\ 0 & \gamma & -k_2-\lambda_3 \end{vmatrix}$$

$$J(E_x) = (-\mu-\lambda_1)\left(\frac{\beta\pi}{\mu}-k_1-\lambda_2\right)(-k_2-\lambda_3) = 0$$

If $-\mu-\lambda_1 = 0 \Rightarrow \lambda_1 = -\mu < 0$

If $\lambda_3 - k_2 = 0 \Rightarrow \lambda_3 = -k_2 < 0$

and if $\frac{\beta\pi}{\mu} - k_1 - \lambda_2 \Rightarrow \lambda_2 = \frac{\beta\pi}{\mu} - k_1$

for λ_2 to be less than zero

$$\Rightarrow \frac{\beta\pi}{\mu} - k_1 < 0$$

$$\Rightarrow \frac{\beta\pi}{\mu} < k_1 \qquad \ldots. (3.27)$$

$$\frac{\frac{\beta\pi}{\mu}}{k_1} < \frac{k_1}{k_1}$$

$$\Rightarrow \frac{\beta\pi}{k_1\mu} < 1,\ \lambda_3 < 0, \text{ where } R_0 = \frac{\beta\pi}{k_1\mu}$$

This indicates that the DFE is locally asymptotically stable if $\frac{\beta\pi}{\mu k_1} < 1 \ldots$

$\frac{\beta\pi}{\mu k_1 = R_0} < 1$ then DFE is locally asymptotically stable.

Theorem (III): The disease free equilibrium E_* of the model is locally asymptotically stable (LAS) if $R_0 < 1$.

Prof: see e. g Kumour (2012)

(3.5) Local Stability of Endemic Equilibrium State

From the linearization of our model used above, we have the Jacobian matrix as

$$\begin{pmatrix} -(\beta y+\mu)-\beta x & & 0 \\ \beta y & \beta x-(\gamma+\mu) & 0 \\ 0 & \gamma & -(\mu+\delta) \end{pmatrix}$$

$$J(E_{88}) = \begin{vmatrix} (-\beta y+\mu)-\lambda_1 & -\beta x & 0 \\ \beta y & \beta x-(r+\mu)-\lambda_2 & 0 \\ 0 & \gamma & -(\mu+\delta)-\lambda_3 \end{vmatrix}$$

we set

$$(\beta y+\mu) = A$$
$$\beta x-(\gamma+\mu) = B$$
$$(\mu+\delta) = C$$

without loss of generality, therefore

$$\begin{vmatrix} -A-\lambda & -\beta x & 0 \\ \beta y & -\beta-\lambda & 0 \\ 0 & \gamma & -c-\lambda \end{vmatrix} = 0$$

$$\begin{vmatrix} -(A+\lambda_1) & -\beta x & 0 \\ \beta y & -(\beta+\lambda_2) & 0 \\ 0 & \gamma & -(C+\lambda_3) \end{vmatrix}$$

$$(A+\lambda_1)\{(B+\lambda_2)(C+\lambda_3)\} - \beta_x\beta_y(C+\lambda_3) = 0$$
$$\Rightarrow (A+\lambda_1)(BC+B\lambda_3+C\lambda_2+\lambda_2\lambda_3)$$
$$-\beta_x\beta_y C - \beta_x\beta_y\lambda_2 = 0$$

We set $\lambda_1 = \lambda_2 = \lambda_3 = \lambda$

$$ABC + A(B+C)\lambda + A\lambda^2 + BC\lambda + (B+C)\lambda^2$$
$$+\lambda^3 + \beta_x\beta_y C + \beta_x\beta_y\lambda = 0$$
$$\lambda^3 + (A+B+C)\lambda^2 + (AB+AC+BC+\beta_X\beta_Y)\lambda$$
$$+ ABC + \beta_X\beta_Y C = 0$$
$$\ldots. (3.28)$$

From equation (3.28) we discovered that $\lambda > 0$ indicating that $\lambda_1 > 0, \lambda_2 > 0, \lambda_3 > 0$ which indicates the disease is endemic in the population.

Conclusion

From our investigation, we observed that the disease free equilibrium (DFE) is locally asymptotically stable for our model when the basic reproduction number of R_0 is $R_0 < 1$ and when $R_0 > 1$ the disease will be endemic.

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