CONTINUOUS–TIME MARKOV CHAIN MODEL FOR TRANSMISSION DYNAMICS OF HIV–INFECTION AND AIDS EPIDEMICS

M. A. Umar
Department of Mathematical Sciences,
Nasarawa State University, PMB 1022, Keffi, Nigeria

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Abstract

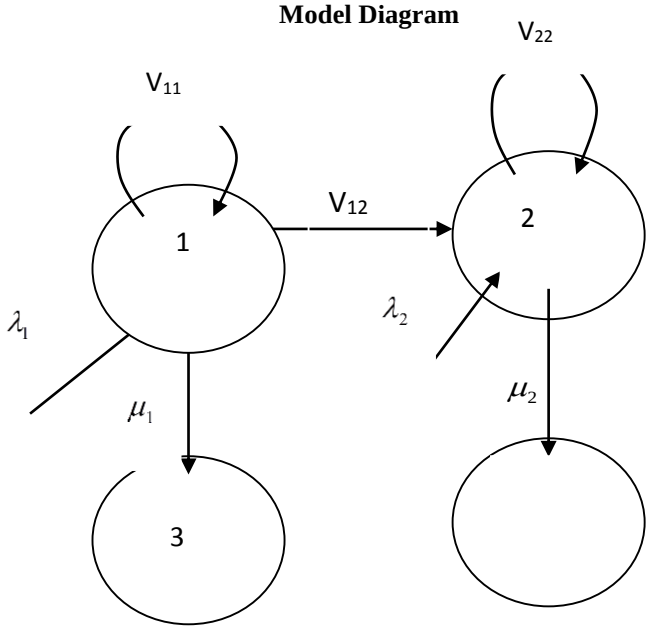
In his work, I developed a continuous time Markov chain model to examine the transmission pattern of HIV–infection between the infectious (symptomatic) and AIDS disease states in a single patch. Using the method of probability generating function, we then derived expressions for the mean numbers of symptomatic and AIDS individuals in these states at any time t.

***Keywords**: HIV infection, Transition intensity.*

INTRODUCTION

HIV and AIDS Pandemic are now entering its second decade. However projection of its future is uncertain, but it is clear from available resources and information that the world wide pandemic is still in its early stages. However, World health organization report for year 1991 shows that the cumulative number of HIV–infection will be 30 to 40 million by year 2000, and that there will be 1 million adult AIDS cases and death per year, with about ½ million in Africa and ¼ million in Asia (Hethcote *et al.*, 2002). These historical scenarios calls for concern and the need for a review of the current intervention methods so as to come up with appropriate policies that will help solve this problem. However it is also recognized by Word health organization that transmission of the HIV virus in Africa and some part of continents are mainly through heterosexual and mother to child modes. With adequate therapies now available to pregnant mothers, cases of Mother to child transmission can now be handled in most hospitals and health centers. Other intervention methods have to be developed to counter the continued increase in the cases of HIV infection through heterosexual contact. In this work we developed a continuous time Markov chain model to study the transmission of HIV–infection through heterosexual contact, and to examine the growth pattern of the disease in the two disease states

Model Diagram



Where,
Stage 1: Symptomatic Stage
Stage 2: HIV– Infectious Stage
Stage 3: Natural (Non Aid Induced) Death stage

Model Assumptions
We assumed the following,

(i) The recruitment, immigration intensities and the intensities of transition from one state to the other, and that of deaths from each state are constant.
(ii) The immigration rates are assumed to be independent of the size of the state.
(iii) The transition intensities of an individual are independent of those of any other individual and are dependent on the size of the state.
(iv) The intensities of death of an individual is depended on the size of the state and are independent of any other individual.
(v) The immigration rate is independent of the size of the state.
(vi) Transitions from AIDS to HIV infectious, susceptible or from HIV infectious state to susceptible states are irreversible, since there are no cures for HIV and AIDS, infectious individuals will eventually die of the infection through the opportunistic diseases.

Model Formulation:
We define the following in line with Chiang (1968); Bailey (1964); Rao (2006); Waema & Olowofeso (2005),

$\lambda^*_i \Delta t + 0(\Delta t)$ = the probability that an increase in population will occur in state i during the time interval, $(t, t + \Delta t)$, through birth and immigration

$\nu^*_{ij} \Delta t + 0(\Delta t)$ = the probability that one individual will move from state α to state β during the time interval (t, t + Δt), through internal immigration.

$\mu^*_i \Delta t + 0(\Delta t)$ = the probability that a decrease in population will occur in state α , during the time interval $(t, t + \Delta t)$, through death and emigration.

$1 + \nu_{ii} \Delta t + 0(\Delta t)$ is the probability that the size of state i will remain unchanged during the time interval $(t, t + \Delta t)$.

For notational convenience, we define in line with Chiang (1968); Waema & Olowofeso (2005); Bailey (1964),

$$\nu^*_{ii} = -[\sum_{j=1, \neq i}^{3} \nu^*_{ij} + \mu^*_i], \ i = 1, 2.,$$

We consider an immigration process in which an increase in population during the time interval (t, t + Δt), is independed of the existing population size. For the state S_i $i = 1,2$, we have

(1) $$\lambda_i^*(t) = \lambda_i, \ \nu^*_{ij} = n_i \nu_{ij}, \ \ \mu^*_i = n_i \mu_i \ \ i = 1, 2$$

(2) $$\nu^*_{ii} + (\sum_{\substack{j=1 \\ j \neq i}}^{3} \nu_{ij} + \mu_i) = 0 \ \ i, j = 1, \ 2.$$

Where $n_i(t)$ is the population size of state i at time t. and

$\lambda_i(t)$ is the immigration rate into state i

$\nu_{ij}(t)$ is the internal immigration rate from state i to state j

$\mu_i(t)$ is the emigration rate from state i

$\kappa_{0,1}$, κ_{02}, respectively and the size of states, S_1, S_2 are κ_1, κ_2 at time t,

Let probability function of the population size of the states at time t be,

(3) $$P_{k_1 k_2}(t) = \Pr ob(X_1(t) = k_1, \ X_2(t) = k_2 / X_1(0) = k_{01}, \ X_2(0) = k_{02})$$

Where $k_1, \ k_2 = 0,1,2,...,(k_{01} + k_{02})$

Using transition intensities, death, immigration and emigration rates into and out of these states. The probability of the size of states $S_1,\ S_2$ at time $(t+\Delta t)$ is,

$$P_{k_1k_2}(t+\Delta t) = P_{k_1-1,k_2}(t)(\lambda_1\Delta t + 0(\Delta t)) + P_{k_1k_2-1}(t)(\lambda_2\Delta t + 0(\Delta t)) + P_{k_1k_2}(t)(1 + k_{11}v_{11}\Delta t + k_{22}v_{22}\Delta t + 0(\Delta t))$$

$$+ \mathrm{P}_{k_1+1k_2-1}(t)((k_1+1)v_{12} + 0(\Delta t)) + P_{k_1+1,k_2}(\mu_1\Delta t + 0(\Delta t)) + P_{k_1k_2+1}(\mu_2\Delta t + 0(\Delta t))$$

$$P_{k_1k_2}(t+\Delta t) - P_{k_1k_2}(t) = P_{k_1k_2}(t)(v_{11}\Delta t + v_{22}\Delta t + 0(\Delta t)) + P_{k_1-1k_2}(\lambda_1\Delta t + 0(\Delta t)) + P_{k_1k_2-1}(t)(\lambda_2\Delta t + 0(\Delta t))$$

$$+ \mathrm{P}_{k_1+1k_2-1}(t)(k_1+1)v_{12}\Delta t + 0(\Delta t)) + P_{k_1+1,k_2}(t)((k_1+1)\mu_1\Delta t + 0(\Delta t)) + P_{k_1k_2+1}(t)((k_2+1)\mu_2\Delta t + 0(\Delta t))$$

The Chapman– Kolmogorov differential equation is,

$$\frac{d}{dt}P_{k_1k_2}(t) = P_{k_1-1k_2}(t)\lambda_1 + P_{k_1k_2-1}(t)\lambda_2 + P_{k_1k_2}(t)\left(k_{11}v_{11} + k_{22}u_{22}\right) \tag{4}$$

$$+ P_{k_1+1k_2}(t)(k_1+1)v_{12} + P_{k_1+1k_2}(t)(k_1+1)\mu_1 + \mathrm{P}_{k_1k_2+1}(t)(k_2+1)\mu_2$$

We solve this differential equation using the method of probability generating function.

Let the joint probability generating function of the sizes of the disease states be,

$$G(S_1,S_2;t) = E(S_1^{k_1}S_2^{k_2}) = \sum_{k_1k_2}P_{k_1k_2}(t)S_1^{k_1}S_2^{k_2} \tag{5}$$

Where

$$\frac{\partial G(S_1,S_2;t)}{\partial t} = \sum_{k_1k_2}\frac{d}{dt}P_{k_1k_2}(t)S_1^{k_1}S_2^{k_2},\quad \frac{\partial G(S_1,S_2;t)}{\partial S_1} = \sum_{k_1k_2}k_1P_{k_1k_2}(t)S_1^{k_1-1}S_2^{k_2},$$

$$\frac{\partial G(S_1,S_2;t)}{\partial S_2} = \sum_{k_1k_2}k_2P_{k_1k_2}(t)S_1^{k_1}S_2^{k_2-1}$$

Using equation (5), with the Chapman–Kolmogorov equation we get the associated partial differential equation,

$$\frac{\partial G(S_1,S_2;t)}{\partial t} = (v_{11}S_1 + v_{12}S_2 + \mu_1)\frac{\partial G}{\partial S_1} + (v_{22}S_2 + \mu_2)\frac{\partial G}{\partial S_2} + (\lambda_1S_1 + \lambda_2S_2)G \tag{6}$$

The auxiliary equations are,

$$-\frac{dt}{1} = \frac{dS_1}{v_{11}S_1 + v_{12}S_2 + \mu_1} = \frac{dS_2}{v_{22}S_2 + \mu_2} = \frac{dG}{(\lambda_1S_1 + \lambda_2S_2)G} \tag{7}$$

Using, $\mu_1 = -v_{11} - v_{12},\quad \mu_2 = -v_{22},\qquad \mathrm{Z}_j = 1 - S_j,\qquad \mathrm{dZ_j} = -dS_j$

The auxiliary equation reduces to,

(8) $\qquad dt \qquad dZ_1 \qquad dZ_2 \qquad dG$

$\overline{Z_2)G}$

From equation (8) we have,

$$\frac{dZ_1}{dt} = -v_{11}Z_1 - v_{12}Z_2 \tag{9}$$

$$\frac{dZ_2}{dt} = -v_{22}Z_2 \tag{10}$$

$$G(Z_1,Z_2;t) = C\exp(-(\lambda_1Z_1 + \lambda_2Z_2)) \tag{11}$$

In matrix representation, equations (9) and (10) can be writhen as,

(12) $$\dot{Z} = AZ$$

Where, A is the matrix coefficients of the system, and Z is a column vector defined respectively by,

$$A = \begin{pmatrix} -v_{11} & -v_{12} \\ 0 & -v_{22} \end{pmatrix}, \qquad Z = (Z_1, Z_2)^t$$

Equations (9) and (10) has the general solution of the form,

(13) $$Z = \alpha \exp(\beta t)$$

Where α the constant of integration and β are the roots of the equation,

(14) $$(\beta I - A) = 0$$

Also, I is the identity matrix of the same order as, A.

Using equation (14) we get the matrix and the corresponding characteristics equation,

$$\begin{pmatrix} -(v_{11} + \beta) & -v_{12} \\ 0 & -(v_{22} + \beta) \end{pmatrix} = 0$$

$$(v_{11} + \beta)(v_{22} + \beta) = 0\ , \qquad \beta_1 = -v_{11}, \qquad \beta_2 = -v_{22}.$$

We find the corresponding eigenvectors as,

Substitute $\beta_1 = -v_{11}$ and $\beta_2 = -v_2$, into equation $(\beta I - A)Z = 0$, gives

$Z = (1,\ 0)^t$ and $Z = (,\frac{v_{11}}{v_{22} - v_{11}},\ \ 1)^t$ respectively.

(15) $$Z = \alpha_1 \begin{pmatrix} 1 \\ 0 \end{pmatrix} e^{-v_{11}t} + \alpha_2 \begin{pmatrix} 1 \\ \frac{v_{11}}{v_{22} - v_{11}} \end{pmatrix} e^{-v_{22}t}$$

(16) $$Z_1 = \alpha_1 e^{-v_{11}t} + \alpha_2 e^{-v_{22}t}$$

(17) $$Z = \frac{v_{11}\alpha_2}{} e^{-v_{22}t}$$

Solving for α_1, and α_2 respectively gives,

(18) $$\alpha_1 = (Z_1 - \frac{v_{11}}{v_{22} - v_{11}} Z_2) e^{v_{11}t}, \qquad \alpha_2 = \frac{v_{11}}{v_{22} - v_{11}} Z_2 e^{v_{22}t}$$

From equation (11) we have,

(19) $$G(Z_1, Z_2; t) = \Phi(\alpha_1, \alpha_2) \exp(-(\alpha_1 Z_1 + \alpha_2 Z_2))$$

Where $\Phi(\alpha_1, \alpha_2)$ is an auxiliary function to be determined using the initial population size of the disease states.

(20) $$G(S_1, S_2; 0) = S_1^{k_{01}} S_2^{k_{02}}$$

Using $Z_j = 1 - S_j$, $j = 1,\ 2,$ gives the joint probability generating function of the size of each of the disease states.

(21) $$G(Z_1, Z_2; 0) = \prod_{j=1}^{2} (1 - Z_j)^{k_{0j}}$$

Where k_{0j} is initial size of state j at time zero

(22) $$\Phi(\alpha_{01}, \alpha_{02}) = \prod_{j=1}^{2} (1 - Z_j)^{k_{0j}} .$$

and $\alpha_{01},\ \alpha_{02}$ are the values of $\alpha_j,\ \mathrm{j} = 1,\ 2.$ at time zero.

Putting these values into the into equations for α, gives the following expressions,

(23) $$\alpha_{01} = Z_1 - \frac{v_{11}}{v_{22} - v_{11}} Z_2, \qquad \alpha_{02} = \frac{v_{11}}{v_{22} - v_{11}} Z_2$$

We solve these equations for Z_j as,

(24) $$Z_1 = \alpha_{01} + \alpha_{02}, \qquad \mathrm{Z}_2 = \frac{v_{22} - v_{11}}{v_{11}} \alpha_{02}$$

The required expression for the auxiliary function Φ is,

(25) $$\Phi(\alpha_{01}, \alpha_{02}) = \prod_{j=1}^{2} (1 - Z_j)^{k_{0j}} .$$

Where Z_j are obtained in equation (24)

The joint probability generating function using equation (25) reduces to,

(26) $$G(Z_1, Z_2; t) = \prod_{j=1}^{2} (1 - Z_J)^{k_{0j}} \exp(-(-(\lambda_1 \alpha_1 + \lambda_2 \alpha_2))$$

For any $t > 0$, the expression for Z_j can be represented as,

$v_{22} - v_{11}$

The auxiliary function Φ, is then represented using equation (27) as,

(28) $$\Phi(\alpha_1,\ \alpha_2) = \prod_{j=1}^{2} (1 - \pi_j)^{k_{0j}}$$

Substituting the values of α_j into equation (27) and simplifying gives the values of $\pi_j,\quad \mathrm{j} = 1, 2.$

(29) $$\pi_1 = Z_1 e^{v_{11} t} + \frac{v_{11}}{v_{22} - v_{11}} Z_2 (e^{v_{22} t} - e^{v_{11} t}), \quad \pi_2 = Z_2 e^{v_{22} t} .$$

We representations the transition probabilities as follows,

(30) $$\sigma_{11} = e^{v_{11}t}, \qquad \sigma_{12} = \frac{v_{11}}{v_{22} - v_{11}}(e^{v_{22}t} - e^{v_{11}t}), \qquad \sigma_{22} = e^{v_{22}t}$$

Where σ_{ij} the probability of are transitions from state i to state j at time t.

The values of π_j can then be writhen as,

(31) $$\pi_1 = \sigma_{11}(t)Z_1 + \sigma_{12}(t)Z_2, \quad \pi_2 = \sigma_{22}(t)Z_2$$

The joint probability generating function of the population size of the states are,

(32) $$G(Z_1, Z_2; t) = \prod_{j=1}^{2}(1-\pi_j)^{k_{0j}} \exp(-(\lambda_1\alpha_1 + \lambda_2\alpha_2))$$

$$G(Z_1, Z_2; t) = \{1-(\sigma_{11}(t)Z_1 + \sigma_{12}(t)Z_2)\}^{k_{01}}\{(1-\sigma_{22}(t)Z_2)\}^{k_{02}} \exp(-(r_1Z_1 + r_2Z_2))$$

$$\mathrm{r}_1 = \lambda_1 te^{v_{11}t}, \qquad \mathrm{r}_2 = \frac{v_{11}}{v_{22} - v_{11}}t(\lambda_2 e^{v_{22}t} - \lambda_1 e^{v_{22}t})$$

Using $Z_j = 1 - S_j$, we obtained the following expressions for the joint probability generating function as,

(33) $$G(S_1, S_2; t) = (\Psi_1(t) + \sum_{j=1}^{2}\sigma_{1j}(t)S_j)^{k_{01}} x (\Psi_2(t) + \sigma_{22}(t))^{k_{02}} \exp(\sum_{j=1}^{2} r_j - \sum_{j=1}^{2} r_j S_j)$$

Where,

$$1 - \pi_1 = 1 - \sigma_{11}(t)Z_1 - \sigma_{12}(t)Z_2 = 1 - \sum_{j=1}^{2}\sigma_{1j}(t) + \sum_{j=1}^{2}\sigma_{1j}(t)S_j = \Psi_k(t) + \sum_{j}^{2}\sigma_{kj}(t)S_j$$

$$\Psi_k(t) = 1 - \sum_{j=1}^{2}\sigma_{kj}(t).$$

The mean and variance of the size of the disease states at any time t are then,

(34) $$E(k_1(t)) = \frac{\partial G(S_1, S_2; t)}{\partial S_1}/_{S_j = 1}, \; \mathrm{j} = 1,2.$$

$$= (\sigma_{11}(t)k_{01}C_1^{k_{01}-1} - r_1C_1^{k_{01}})C_2^{k_{02}}$$

(35) $$Var(k_1(t)) = E(k_1(t)(k_1(t) - 1)) + E(k_1(t)) - [E(k_1(t))]^2$$

(36) $$E(k_2(t)) = k_{02}\sigma_{22}(t)C_1^{k_{01}}C_2^{k_{02}} + k_{01}\sigma_{12}(t)C_1^{k_{01}}C_2^{k_{02}} - r_2C_1^{k_{01}}C_2^{k_{02}}$$

(37) $$Var(k_2(t)) = (k_{02} - 1)k_{02}\sigma_{22}^{2}(t)C_1^{k_{01}}C_2^{k_{02}-2} + 2k_{01}k_{02}\sigma_{12}(t)C_1^{k_{01}-1}C_2^{k_{02}-1}$$

$$+ (k_{01} - 1)k_{01}\sigma_{12}^{2}(t)C_1^{k_{01}-2}C_2^{k_{02}} - 2\mathrm{r}_2k_{02}\sigma_{22}C_1^{k_{01}}C_2^{k_{02}-1} + k_{01}\sigma_{12}(t)C_1^{k_0-1}C_2^{k_{02}}$$

Where,

$$C_1 = \psi_1(t) + \sum_{j=1}^{2}\sigma_{1j}(\mathrm{t}), \qquad C_2 = \psi_2(t) + \sigma_{22}(t)$$

DISCUSSION

The expected population size of the two disease states and their spread can be estimated at any time t, using equations (34) – (37). These expressions will help us to determine the growth rate of the two states, and will also guide policy makers on health on the appropriate intervention methods to be adopted, so as to reduce the level of transmission of the disease in the population.

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