TRACING THE HIGH RISK POPULATION OF HIV THROUGH CUMULATIVE MODEL

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ABSTRACT

The time to cross the threshold of the infected person is a vital event in seroconversion. Modeling in Statistics should always be biologically correct and the extent of approximations should be clear in model development. So, any biostatistical model of a complex biological phenomenon not only need to be an approximation of real world but also has to be addressed to a specific target, to respond a precise question about the phenomenon. Namely, HIV models are used to estimate specific immuno-virological parameters, an optimized therapy or the expected number of newly infected cells. We propose a stochastic model to study the damage process acting on the immune system that is non-linear. The mean of seroconversion time of HIV is derived. A numerical example is given to illustrate the seroconversion times of HIV transmission.

Keywords: Antigenic diversity threshold, Seroconversion, Human Immuno efficiency Virus. Acquired Immuno Deficiency Syndrome. Alpha poisson Process. Mittag-Leffler distribution.

1. INTRODUCTION

One of the most urgent public-health problems in developing countries is the AIDS (Acquired Immune Deficiency Syndrome) epidemic, caused by the Human Immuno deficiency Virus (HIV). Since the first cases of AIDS were identified in 1981, the number of HIV infected people and AIDS deaths per year has continued to rise rapidly. In 2004, some 40 million people were living with HIV, which has killed over 20 million since 1981 and 3 million in 2003 alone, [1]. [2] a non-linear mathematical model for HIV epidemic spreads through both horizontal and vertical transmission, in a variable size of population. Vertical transmission can be successful through transplantal transfer of disease agent. A few studies of vertical transmission have been recently conducted to describe the effects of the epidemiological and demographical factors [3, 4, 5, 6, 7, 8]. The authors have given in this paper a model for HIV transmission into a different size of population with vertical transmission and other demographic and epidemiological factors.

2. DESCRIPTION OF STOCHASTIC MODEL

Let us consider a susceptible population whose major mode of transmission is through heterosexual activity. Assume that at time t=0, a new member of tested HIV negative enters the population and makes sexual contacts with member of susceptible. Let the sexual contacts occur at random time points which is assumed to follow the Alpha Poisson distribution [9] with parameters ‘a’ and ‘α’ which is given as

\[ P_{a,\alpha}(n,t) = \sum_{k=0}^{\infty} \frac{(-1)^k}{k!} \frac{(at)^{\alpha(k+n)}}{\Gamma(\alpha(k+n)+1)}, \quad a > 0, 0 < \alpha < 1, \quad n = 0,1,2, \ldots \]

\[ = e^{-(at)^{\alpha}} \frac{(at)^{\alpha}}{\Gamma(\alpha(k+n)+1)}, \quad a > 0, 0 < \alpha < 1 \]

Let G(t) bee the distribution function of the interarrival between the contacts which follows Mittag-Leffler distribution. The distribution function of Mittag-Leffler distribution [10] is given by

\[ G_{a,\alpha}(t) = \sum_{k=0}^{\infty} \frac{(-1)^k}{\Gamma(\alpha(k+n)+1)} (at)^{\alpha}, \quad t \geq 0, \quad a > 0, 0 < \alpha \leq 1 \]
Let the seroconversion time of the HIV of the individual be represented by the random variable $T$. We obtain the seroconversion distribution of HIV by a stochastic model based on the following assumptions.

i) Sexual contact is the only source of HIV transmission.

ii) An uninfected individual has sexual contacts with a HIV infected partner.

iii) Damages to individuals are caused by transmission of HIV at each contact and the interarrivals between the contacts are independent identically distributed random variables.

iv) The damage process acting on the immune system of an infected individual is non-linear and cumulative.

v) The total damage caused exceeds a threshold level $Y$ which itself is a random variable, the seroconversion and the person is recognized as infected.

vi) The process that generates the contacts, the sequence of damages and threshold are mutually independent.

Let $X_i$ be the antigenic diversity arising due to HIV transmission during the $i^{th}$ contact and $X_i$s are i.i.d for $i=1, 2, \ldots, k$

$G(.) = \text{The c.d.f of X by taking } X_i = X \text{ for } i=1, 2, \ldots, k$

$G(.) = \text{The probability density function of } X_i$

$V_k(t) = \text{The probability of exactly k contacts in (0, t]}$

$g^*(s) = \text{Laplace transform of } g(x)$

$g_k(.) = \text{The probability density function of random variable } \sum_{0}^{k} X_i$, which is the $k$th convolution of $g(.)$

$Y = \text{Random variable denoting the antigenic diversity threshold, which follows Alpha Poisson distribution with parameter}$

$h(.)= \text{The probability density function of antigenic diversity threshold levels for the two sources, and } Y_1 \sim \exp(\mu_1), Y_2 \sim \exp(\mu_2) \text{ has competing Alpha Poisson distribution with parameters } \mu_1, \mu_2$ so that

$P[Y < y] = 1 - \{e^{(\mu_1)y} + e^{(\mu_2)y} - e^{(\mu_1+\mu_2)y}\}, y > 0, \mu_2 > 0, \mu_1 > 0$

$P[X < Y] = \text{The probability that damaged caused in a single contact is less than the threshold } Y$

$S(t) = P[\text{no infection in (0,t]}] = P[T > t]$

The model parameters are

- $\alpha$ - Contact of the infected partner.
- $\alpha'$ - Intensity of HIV infected partner.
- $\mu$ - Antigenic diversity threshold.

under the above assumptions with non linear damage process acting on the immune system, we have the following theorem.

**Theorem 2.1:** If the number of contacts is an Alpha poisson process with parameters ‘$a$’ and ‘$\alpha$’ and intercontact time is a Mittag-Leffler distribution while the threshold level is an Alpha Poisson distribution with parameter ‘$\mu_1$’, ‘$\mu_2$’, then the probability density function of seroconversion time is a three parameter Weibull distribution

**Proof:**

$S(t) = P[\text{no infection in (0,t]}] = P[T > t]$

$= \sum_{0}^{\infty} P[\text{exactly k contact in (0,t] with intensity } \alpha] * p[\text{exactly k contact in (0,t] with intensity } \alpha']$

$= \sum_{0}^{\infty} V_k(t) P \left\{ \sum_{0}^{\infty} X_i < Y_1, Y_2 \right\}$

Where $V_k(t) = \text{probability of exactly k contacts in (0,t] with intensity } \alpha$ which is the Alpha poisson distribution with parameter ‘$a$’ and ‘$\alpha$’

$= \sum_{0}^{\infty} \frac{e^{-(at)^{\alpha}}(at)^k}{\Gamma(ak+1)}$, $a > 0, 0 < \alpha \leq 1$

$E(T) = \int 0^{\infty} (t) dt$

$= \sum_{0}^{\infty} \frac{e^{-(at)^{\alpha}}(at)^k}{\Gamma(ak+1)}$, $a > 0, 0 < \alpha \leq 1$
The probability of seroconversion time is calculated for the various intervals by defining

\[
P_t = \frac{1}{\Gamma(ak+1)} e^{-\left(\frac{a}{a+\mu} + \frac{1}{a+\mu}ight)^k} \int_0^\infty g^*(\mu_1 + \mu_2) \left(1 - e^{-\left(\frac{a}{a+\mu} + \frac{1}{a+\mu}ight)^k}\right) dt
\]

where \( g^*(\mu_1 + \mu_2) \) Laplace is the Transformation of \( g(x) \)

\[
S(t) = \sum_{i=0}^\infty V_k(t) \left\{ g^*(\mu_1) + g^*(\mu_2) - g^*(\mu_1 + \mu_2) \right\}
\]

\[
L(t) = 1 - S(t) = 1 - \left\{ e^{-\left(a[1-g(\mu_1)]t^\alpha\right)} + e^{-\left(a[1-g(\mu_2)]t^\alpha\right)} - e^{-\left[a\{\frac{1}{a+\mu_1}\}t^\alpha\right]} \right\}
\]

Since the probability density function \( X \), follows Mittag-Leffler, then

\[
g^*(\mu_1) = \frac{a^\alpha}{a^\alpha + \mu_1} \Rightarrow 1 - g^*(\mu_1) = \frac{\mu_1^\alpha}{a^\alpha + \mu_1}
\]

\[
g^*(\mu_2) = \frac{a^\alpha}{a^\alpha + \mu_2} \Rightarrow 1 - g^*(\mu_2) = \frac{\mu_2^\alpha}{a^\alpha + \mu_2}
\]

\[
g^*(\mu_1 + \mu_2) = \frac{a^\alpha}{a^\alpha + (\mu_1 + \mu_2)} \Rightarrow 1 - g^*(\mu_1 + \mu_2) = \frac{\mu_1^\alpha + \mu_2^\alpha}{a^\alpha + (\mu_1 + \mu_2)}
\]

The probability density function of seroconversion time \( T \) is

\[
\Psi(t) = \left\{ \frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)} \right\} dt
\]

\[
\Psi(t) = \left\{ \frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)} \right\} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)}
\]

3. PROBABILITY OF SEROCONVERSION TIME

The probability of seroconversion time is calculated for the various intervals by defining

\[
p_i = \int_{t_i}^{t_{i+1}} \Psi(t) dt \quad for \quad i = 1, 2, 3...
\]

\[
p_i = \int_{t_i}^{t_{i+1}} \left\{ \frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)} \right\} dt \quad for \quad i = 1, 2, 3...
\]

\[
= \frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)} \int_{t_i}^{t_{i+1}} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)} dt +
\]

\[
= \frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)} \int_{t_i}^{t_{i+1}} t^{a-1} e^{-\left(\frac{a^\alpha \mu_1^\alpha a^\alpha \mu_2^\alpha}{(a^\alpha + \mu_1 t^\alpha)(a^\alpha + \mu_2 t^\alpha)}\right)} dt \quad for \quad i = 1, 2, 3...
\]
4. PERFORMANCE MEASURES

The expected time to seroconversion time is \[ E(T) = \int_0^\infty \psi(t) dt \]

The expected time to seroconversion time is \[ E(T) = \int_0^\infty \psi(t) dt \]

\[ A_1 = \frac{\alpha^\alpha \mu_1^\alpha}{a^\alpha + \mu_1^\alpha} \int _0^\infty t \ t^{\alpha-1} \ \left( \frac{\alpha^\alpha \mu_2^\alpha}{a^\alpha + \mu_2^\alpha} \right) dt \]

\[ A_2 = \frac{\alpha^\alpha (\mu_1^\alpha + \mu_2^\alpha)}{a^\alpha + (\mu_1^\alpha + \mu_2^\alpha)} \int _0^\infty t \ t^{\alpha-1} \ \left( \frac{\alpha^\alpha (\mu_1^\alpha + \mu_2^\alpha)}{a^\alpha + (\mu_1^\alpha + \mu_2^\alpha)} \right) dt \]

From A1,

\[ c_1 = \frac{\alpha^\alpha \mu_1^\alpha}{a^\alpha + \mu_1^\alpha} \quad \text{and} \quad \left( \frac{\alpha^\alpha \mu_1^\alpha}{a^\alpha + \mu_1^\alpha} \right) t^\alpha = \frac{y}{c_1} \Rightarrow x = \frac{y}{c_1} \]

\[ t^\alpha = \frac{y}{c_1} \Rightarrow \alpha t^{\alpha-1} dt = \frac{dy}{c_1} \quad \text{and} \quad \alpha t^{\alpha-1} dt = \frac{dy}{c_1} \]

\[ A_1 = \int_0^\infty e^{-\gamma \left( \frac{y}{c_1} \right)^{1/\alpha}} \frac{dy}{c_1} = \frac{1}{c_1^{1/\alpha}} \int_0^\infty e^{-\gamma y^{1/\alpha}} dy = \frac{1}{c_1^{1/\alpha}} \Gamma \left( \frac{1}{\alpha} + 1 \right) \]

From A2,

\[ c_2 = \frac{\alpha^\alpha \mu_1^\alpha}{a^\alpha + \mu_1^\alpha} \quad \text{and} \quad \left( \frac{\alpha^\alpha \mu_1^\alpha}{a^\alpha + \mu_1^\alpha} \right) t^\alpha = \frac{y}{c_2} \Rightarrow x = \frac{y}{c_2} \]

\[ t^\alpha = \frac{y}{c_2} \Rightarrow \alpha t^{\alpha-1} dt = \frac{dy}{c_2} \quad \text{and} \quad \alpha t^{\alpha-1} dt = \frac{dy}{c_2} \]

\[ A_2 = \int_0^\infty e^{-\gamma \left( \frac{y}{c_2} \right)^{1/\alpha}} \frac{dy}{c_2} = \frac{1}{c_2^{1/\alpha}} \int_0^\infty e^{-\gamma y^{1/\alpha}} dy = \frac{1}{c_2^{1/\alpha}} \Gamma \left( \frac{1}{\alpha} + 1 \right) \]

From A3,

\[ c_3 = \frac{\alpha^\alpha (\mu_1^\alpha + \mu_2^\alpha)}{a^\alpha + (\mu_1^\alpha + \mu_2^\alpha)} \quad \text{and} \quad \left( \frac{\alpha^\alpha (\mu_1^\alpha + \mu_2^\alpha)}{a^\alpha + (\mu_1^\alpha + \mu_2^\alpha)} \right) t^\alpha = \frac{y}{c_3} \Rightarrow x = \frac{y}{c_3} \]

\[ t^\alpha = \frac{y}{c_3} \Rightarrow \alpha t^{\alpha-1} dt = \frac{dy}{c_3} \quad \text{and} \quad \alpha t^{\alpha-1} dt = \frac{dy}{c_3} \]

\[ A_3 = \int_0^\infty e^{-\gamma \left( \frac{y}{c_3} \right)^{1/\alpha}} \frac{dy}{c_3} = \frac{1}{c_3^{1/\alpha}} \int_0^\infty e^{-\gamma y^{1/\alpha}} dy = \frac{1}{c_3^{1/\alpha}} \Gamma \left( \frac{1}{\alpha} + 1 \right) \]

The expected value is simplified as

\[ E(T) = \left( \frac{\alpha^\alpha + \mu_1^\alpha}{a^\alpha \mu_1^\alpha} \right)^{1/\alpha} + \left( \frac{\alpha^\alpha + \mu_2^\alpha}{a^\alpha \mu_2^\alpha} \right)^{1/\alpha} - \left( \frac{\alpha^\alpha + (\mu_1^\alpha + \mu_2^\alpha)}{a^\alpha (\mu_1^\alpha + \mu_2^\alpha)} \right)^{1/\alpha} \Gamma \left( \frac{1}{\alpha} + 1 \right) \]
5, CONCLUSION

From the Figure (1), we observed that for fixed $\mu_1, \mu_2$ when 'a' (High Risk Contact rate) increases, the mean of time decreases. Also if 'a' is fixed and $\mu_1, \mu_2$ (Antigenic Diversity threshold) is allowed to increase then the mean time to seroconversion decreases. Also intensity of the human immuno Deficiency virus transmission of the infected partner increases, the mean time to seroconversion time decreases. The practical implication of the result is that the spread of HIV is faster as the intensity of the immune system is lower. The risk population of infected person’s decreases slowly compared with the Exponential curve which is observed in the above figure. The mean of the cumulative quantity of Antigenic threshold decreases with time of risk contact. One can find more related works from [11, 12, 13, 14].

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REFERENCE


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