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# TIME TO SURVIVAL OF HIV ENVIRONMENT OF THE INFECTED PATIENTS

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## Abstract

Survival model for the HIV environment of the infected patients and the model to characterize the HIV infection person with seroconversion time has been studied. Through stimulation generated infection distributions and seroconversion distributions, we assess the effects of various risk factors on these distributions. The model fit of some data suggests that Setting the Clock Back to Zero Property should be assumed as the infection distribution for the proposed stochastic model of HIV epidemics.

**Key Words :** Antigenic Diversity, HIV, Survival, Shock Model, Threshold.

## 1. Introduction

Over the course of the 20th and 21st century, human lifespans increased dramatically in many parts of the world. This reduction in mortality is largely attributed to a reduced burden of infectious diseases, due to improved nutrition and sanitation, and the introduction of both antibiotics and vaccines. We were so confident of our domination over the microbial world that in the mid 20th and 21st century, it was common to surmise the end of infectious diseases as a significant health issue. This sentiment turned out to be especially ill timed, as the last few decades saw the emergence of many novel and extremely dangerous pathogens, including Ebola, SARS, Lyme disease, Legionella, drug-resistant malaria and tuberculosis. Perhaps no disease shattered this view as much as the outbreak of the human immunodeficiency virus (HIV), and the acquired immune deficiency syndrome (AIDS) that it causes.

Infectious diseases remain a formidable challenge to human health, and understanding pathogen evolution is crucial to designing effective therapeutics and control strategies. Here, we review important evolutionary aspects of HIV infection, highlighting the concept of selection at multiple spatial and temporal scales. At the smallest scale, a single cell may be infected by multiple virions competing for intracellular resources. Recombination and phenotypic mixing introduce novel evolutionary dynamics. As the virus spreads between cells in an infected individual, it continually evolves to circumvent the immune system. We discuss evolutionary mechanisms of HIV pathogenesis and progression to AIDS. Viral spread throughout the

human population can lead to changes in virulence and the transmission of immune-evading variation. HIV emerged as a human pathogen due to selection occurring between different species, adapting from related viruses of primates. HIV also evolves resistance to antiretroviral drugs within a single infected host, and we explore the possibility for the spread of these strains between hosts, leading to a drug resistant epidemic. We investigate the role of latency, drug-protected compartments and direct cell-to-cell transmission on viral evolution. The introduction of an HIV vaccine may select for viral variants that escape vaccine control, both within an individual and throughout the population. Due to the strong selective pressure exerted by HIV-induced morbidity and mortality in many parts of the world, the human population itself may be co-evolving in response to the HIV pandemic. Throughout the paper, we focus on trade-offs between costs and benefits that constrain viral evolution and accentuate how selection pressures differ at different levels of selection. Some of the models on HIV/AIDS studies can be found in Chiang (1980), Hethcote (1989), Anderson(1991), Luboobi (1991), Bailey (1996), and Iwunor (1999). A good number of these models are deterministic rather than stochastic in nature. Much work has not been done in the area of HIV/AIDS epidemic by examining the majormodesof transmission: this serves as motivation for this study.

Many studies related to the expected time of the patient have been carried out by many authors. Pradeep Sukla et al (2013) discussed how to prevent the threshold in Human Immune Virus of infected persons through statistical model. Subramanian et al (2012) estimated the expected time in shock model using Generalized Logistic Distribution which shows some interesting results of the infected Human Immune Virus with simulation study. Kannan et al (2011) studied the estimation of expected time to seroconversion of Human Immune Virus infected using order statistics. Pandiyan et al (2010) derived the expected time to attain the threshold level using multisource of Human Immune Virus transmission through shock model approach.

## 2. Fitting of Model

The random variable Y denotes the Antigenic DiversityThreshold.

The p.d.f of Y is given as h(y) and

$$h_1(y) = \mu_1\ e^{\mu_1 y}\ if\ \ y \le y_0\ and\ h_2(y) = \mu_2 e^{\mu_2 y}\ \ e^{y_0(\mu_2-\mu_1)} if\ \ y > y_0$$

Where $y_0\ is\ the\ truncation\ point$ for Y

One is interested in an item for which there is a significant individual variation in ability to withstand shocks. When the immune system is affected in human body, shock with different infected variable is the one to look. Now probability in 'k' contacts in (0,t) the antigenic diversity does not cross the threshold is given by

$$P\left[\sum_{i=0}^{k} X_i < Y\right] = e^{-\mu_1 x} + e^{y_0(\mu_1-\mu_2)} e^{-\mu_2 x} \qquad (1)$$

## 3. 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 (Anil 2001) with parameters 'a' and '$\alpha$' which is given as

$$= \frac{e^{-(at)^{\alpha}}(at^{\alpha})^{k}}{\Gamma(\alpha k+1)} \tag{2}$$

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 by (Anil 2001) and Pillai (1990) is given by

$$G_{a,\alpha}(t) = \sum_{0}^{\infty} \frac{(-1)^{k}(at)^{\alpha}}{\Gamma(\alpha k+1)} \tag{3}$$

Let the seroconversion time of the HIV of the individual represented by the random variable T. we obtain the seroconversion distribution of HIV by a stochastic model based on the following assumptions since there in no practical real life data in Indian scenario.

Sexual contact is the only sources of HIV transmission.An uninfected individual has sexual contacts with a HIV infected partner.Damages to individuals are caused by transmission of HIV at each contact and the interarrivals between the contacts are independent, identically distributed random variables.The damage process acting on the immune system of an infected individual is non-linear and cumulative.The total damage caused exceeds a threshold level Y which itself is a random variable, the seroconversion and the person is recognised as infected.The process that generates the contacts, the sequence of damages and threshold are mutually independent.

One is interested in an item for which there is a significant individual variation in ability to withstand shocks. There may be no practical way to inspect an individual item to determine its threshold y. In this case, the threshold must be a random variable.

$P[Y < y] = e^{-\mu_1 x} + e^{y_0(\mu_1-\mu_2)}e^{-\mu_2 x}$ , $y > y_0, y \leq y_0, \mu_2 > 0, \mu_1 > 0$

$P[X < Y]$ = The probability that damaged caused in asingle contact is less than the threshold Y

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

The model parameters are

a- Contact of the infected partner, α - Intensity of the HIV of the infected partner, μ - Antigenic diversity threshold. under the above (3) assumptions with nonlinear damage process acting on the immune system, we have the following theorem.

### 3.1 Theorem

If the number 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 exponential distribution with parameter '$\mu$' ,then the probability density function of seroconversion time is a three parameter Weibull distribution.

**Proof**

$S(t) = P\{no\ infection\ (0,t]\} = P\{T > t\} = \sum_0^\infty P$[exactly k contact in (0,t] with intensity $\alpha$ ] * p[exactly k contact in (0,t] with intensity $\alpha$]. It may happen that successive shocks become increasingly effective in causing damage, even though they are independent. This means that$V_k(t)$, the distribution function of the k[th] damage is decreasing in k = 1,2, …for each t. A renewal process is a counting process such that the time until the first event occurs has some distribution F, the time between the first and second event has, independently of the time of the first event, the same distribution F, and so on. When an event occurs, we say that a renewal has taken place. It is also known from renewal process that

$$= \sum_0^\infty V_k(t) P\left\{\sum_0^\infty X_i < Y\right\} \tag{4}$$

On simplification we obtain the survival time in equation (5)

$$S(t) = e^{-(at)^\alpha}[1 - g^*(\mu_1)] + e^{y_0(\mu_1-\mu_2)} e^{-(at)^\alpha}[1 - g^*(\mu_2)] \tag{5}$$

Data that measure "the length of time" until the occurrence of an event are called lifetimes, failure times or survival data. $L(t) = 1 - S(t)$

$$L(t) = 1 - \left\{ e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} + e^{y_0(\mu_1-\mu_2)} e^{-\left\{\frac{a^\alpha {\mu_2}^\alpha}{a^\alpha + {\mu_2}^\alpha} t^\alpha\right\}} \right\} \tag{6}$$

Since the probability density function $X_i$ follows Mittag-Leffler, then

$$g^*(\mu_1) = \frac{a^\alpha}{a^\alpha + {\mu_1}^\alpha} \Longrightarrow 1 - g^*(\mu_1) = \frac{{\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}$$

$$g^*(\mu_2) = \frac{a^\alpha}{a^\alpha + {\mu_2}^\alpha} \Longrightarrow 1 - g^*(\mu_2) = \frac{{\mu_2}^\alpha}{a^\alpha + {\mu_2}^\alpha}$$

The probability density function of seroconversion time T is

$$\Psi\Psi(t) = \left\{\frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha}\right\} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} + e^{y_0(\mu_1-\mu_2)} \left\{\frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_2}^\alpha}\right\} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} \tag{7}$$

which is the form of three parameter weibull distribution.

## 4. Probability of Seroconversion Time

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

$$p_i = \int_{t_i}^{t_{i+1}} \Psi\Psi(t)dt \qquad for\ i = 1,2,3\ \ldots$$

$$p_i = \int_{t_i}^{t_{i+1}} \left\{ \left( \frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}\right\}} \right) + e^{y_0(\mu_1-\mu_2)} \left( \frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_2}^\alpha} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}\right\}} \right) \right\} dt \quad for\ i = 1,2,3 \ldots$$

$$t \geq 0, a > 0 > \ ,0 < \alpha \leq 0 \ and\ \mu_1 > 0, \mu_2 > 0$$

$$= \frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} \int_{t_i}^{t_{i+1}} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} dt + e^{y_0(\mu_1-\mu_2)} \frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_2}^\alpha} \int_{t_i}^{t_{i+1}} t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} dt \quad (8)$$

$$Let\ z = \frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha \Rightarrow \alpha t^{\alpha-1} dt = \frac{dz}{\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}} = \frac{dz}{c}, where\ c = \frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}$$

And $$Let\ z = \frac{a^\alpha {\mu_2}^\alpha}{a^\alpha + {\mu_2}^\alpha} t^\alpha \Rightarrow \alpha t^{\alpha-1} dt = \frac{dz}{\frac{a^\alpha {\mu_2}^\alpha}{a^\alpha + {\mu_2}^\alpha}} = \frac{dz}{c}, where\ c = \frac{a^\alpha {\mu_2}^\alpha}{a^\alpha + {\mu_2}^\alpha}$$

## 5. Performance Mesures

The expected time to seroconversion time is

$$E(T) = \int_0^\infty \Psi\Psi(t) d\, t$$

$$= \frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} \int_0^\infty t \ \ t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_1}^\alpha \alpha}{a^\alpha + {\mu_1}^\alpha} t^\alpha\right\}} dt + \ e^{y_0(\mu_1-\mu_2)} \frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_2}^\alpha} \int_0^\infty t \ \ t^{\alpha-1} e^{-\left\{\frac{a^\alpha {\mu_2}^\alpha \alpha}{a^\alpha + {\mu_2}^\alpha} t^\alpha\right\}} dt \quad (9)$$

$E(T) = A_1 + A_2$

From $A_1$,

$$Let\ c_1 = \frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha} \text{ and } \left(\frac{a^\alpha {\mu_1}^\alpha}{a^\alpha + {\mu_1}^\alpha}\right) t^\alpha = \text{y then}$$

$$t^\alpha = \frac{\text{y}}{c_1} \Rightarrow \alpha\, t^{\alpha-1}\, \text{dt} = \frac{\text{dy}}{c_1} \text{ and } \alpha\, t^\alpha \text{dt} = \left(\frac{\text{y}}{c_1}\right)^{\frac{1}{\alpha}} \frac{\text{dy}}{c_1}$$

$$\therefore \ A_1 = \int_0^\infty e^{-y} \left(\frac{y}{c_1}\right)^{1/\alpha} \frac{\text{dy}}{c_1} = \frac{1}{{c_1}^{1/\alpha}} \int_0^\infty e^{-y} y^{1/\alpha}\, dy = \frac{1}{{c_1}^{1/\alpha}} \Gamma\left(\frac{1}{\alpha} + 1\right)$$

Similarly $A_2$, is obtained as

$$\therefore \ A_2 = \int_0^\infty e^{-y} \left(\frac{y}{c_2}\right)^{1/\alpha} \frac{\text{dy}}{c_2} = \frac{1}{{c_2}^{1/\alpha}} \int_0^\infty e^{-y} y^{1/\alpha}\, dy = \frac{1}{{c_2}^{1/\alpha}} \Gamma\left(\frac{1}{\alpha} + 1\right)$$

The expected survival time obtained

$$E(T) = \left\{ \left( \frac{a^{\alpha} + {\mu_1}^{\alpha}}{a^{\alpha}{\mu_1}^{\alpha}} \right)^{1/\alpha} + e^{y_0(\mu_1 - \mu_2)} \left( \frac{a^{\alpha} + {\mu_2}^{\alpha}}{a^{\alpha}{\mu_2}^{\alpha}} \right)^{1/\alpha} \right\} \Gamma\left( \frac{1}{\alpha} + 1 \right) \qquad (10)$$

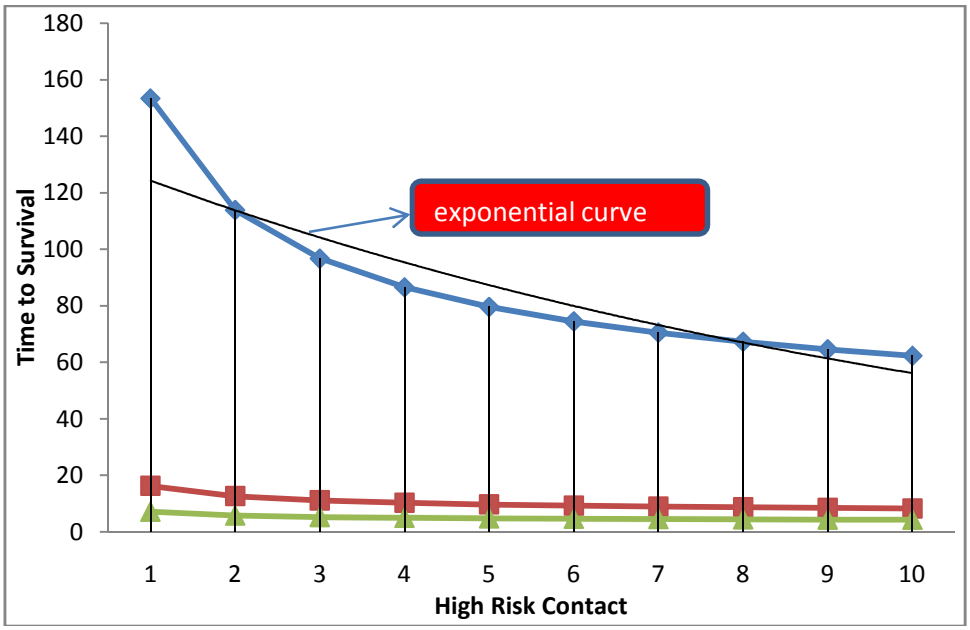


**Figure 1**

## 6. Discussion

From the figure 1 we observed that for fixed $'\alpha'$, '$y_0$' as $'\mu_1'$, $\mu_2'$,and 'a' (constant rate) increases, the mean of seroconversion 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 if $'\alpha'$ and 'a' are fixed and $\mu_1', \mu_2'$ (Antigenic diversity thresholds) is allowed to increase then the mean time to seroconversion decreases. Also if the intensity of the HIV of the infected partner increases, the expected 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.

It is quite interesting to observe that the changes in the distribution of the random variable denoting the antigenic diversity threshold is purely dependent on the natural immune ability posed by an individual and it changes from one to another person. The behaviour of the individuals is explained by the inter-arrival times between successive contacts. This also influences the time to seroconversion. Again the infectiousness of the partner is a major contributory factor to antigenic diversity in successive contacts. The parameter of this random variable also influences the values of expected time and variance time. Hence the physiological structure of the immune system, an ability of an individual and number of successive contacts are all responsible for the time to seroconversion.

It is quite important to observe that the distributions are taken only for the purpose of mathematical explanation of the models but to make the models application oriented in real life situations, it is quite essential to collect all medical data from the infected persons and to examine goners of fit of the distributions which could be filtered to the data otherwise the models will be conveying wrong information of the exact distribution of the antigenic diversity threshold measuring the antigenic diversity contribution in every contact are practically very difficult if not impossible.

Finally, it would be real contribution to the development of this area of study if distributions denoting the various random variables are approximately fixed. Research could be application oriented means of collecting real life data from the affected respondents. It is better to choose the distribution of such random variables which would be able to portray real life conditions.

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