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Research Article

A STOCHASTIC MODEL WITH ANTIGENIC DIVERSITY THRESHOLD OF HIV TRANSMISSION USING SMALLEST ORDER STATISTICS

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ABSTRACT

This paper focuses on the study of a stochastic model for predicting the excepted time to cross the antigenic diversity threshold of HIV infected using the intercontact time between the successive contact forms an order statistics. In the estimation of excepted time to seroconversion, there is an important role for the interarrival time between successive contact and its has a significance influence. We propose the stochastic model assuming the intercontact time between successive contact from a smallest order statistics and threshold distribution is Generalized Rayleigh Distribution. The mean time to seroconversion and its variance are derived and numerical illustrations are provided.

INTRODUCTION

One of the crucial points that has to be made about the HIV/AIDS epidemic is that it is different from most other epidemics and diseases. AIDS stands for Acquired Immune Deficiency Syndrome which is caused by Human Immunodeficiency Virus. In the study of HIV infection and its progression, the antigenic diversity of the antigen namely the HIV plays an important role. The intensity of sexual contact is an important factor that adds to the antigenic diversity since more number of new antigens are acquired by the individual who is getting infected. The time to seroconversion from the point of infection depends upon what is known as antigenic diversity, which acts against immune ability of an individual. The antigenic diversity threshold is a particular level of the antigenic diversity, above which the immune system is unable to suppress the virus population. According to Stiliankis *et al*. (1994) 'the total virus population may escape control through continued generation of new mutants until the total number of different HIV strains exceeds the diversity threshold'. This model predicts unrestrained HIV replication, which includes transmission of more and more HIV in successive contacts and the simultaneous depletion of CD4 cells, the immune system of human body is completely suppressed which in turn leads to seroconversion.

Mathematical methods have been developed by Nowak and May (1991), and Kirschner *et al*. (2000) developed suitable model to estimate the antigenic diversity threshold. Sathiyamoorthi and Kannan (2001) used the shock model and cumulative damage process evolved by Esary *et al*. (1973) to estimate the expected time to cross the antigenic diversity threshold. In the estimation of expected time to seroconversion there is an important role for interarrival times between successive contacts; and it has a significant influence. In the case of persons exposed to HIV infection through sexual contacts, the contribution to the antigenic diversity would depend upon the number of contacts in the interval (0, t].

Ratchagar *et al*. (2003) have derived a model for the estimation of expected time to seroconversion of HIV infected using order statistics. Kannan *et al*. (2008, 2009, 2013, 2015 and 2016) have obtained a stochastic model for estimation of expected time to seroconversion of HIV infected using order statistics and threshold follows Gamma, Erlang-2, Exponentiated Exponential, Exponentiated Modified Weibull, Exponential-Geometric distribution. In this paper, it is assumed that the

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threshold follows Generalized Rayleigh distribution and interarrival times form an order statistics; and so they are not independent. This is due to the fact that if the smallest order statistics is taken, it implies that the interarrival times are becoming smaller. Hence frequent contacts would be possible which will have its impact on the time to seroconversion. In this study, the theoretical results are substantiate using numerical data.

Assumptions of the model

The following are the assumptions underlying in the model developed here

- The transmission of HIV is only through sexual contacts.
- An uninfected individual has sexual contacts with HIV infected partner, and a random number of HIV are getting transmitted, at each contact.
- An individual is exposed to a damage process acting on the immune system and the damage is assumed to be linear and cumulative.
- The interarrival times between successive contacts are taken to be identically and independently distributed random variables.
- The sequence of successive contacts and threshold level are independent.
- From the collection of large number of interarrival times between successive contacts of a person, a random sample of 'k' observations are taken.

Notations

The notations used in this model are as follows

X_i : a random variable denoting the amount of damage arising due to i^{th} contact $X_i^{'s}$ are identically and independently distributed with p.d.f. $g(.)$ and c.d.f. $G(.)$.

Y : a random variable representing the antigenic diversity threshold which follows Generalized Rayleigh distribution with parameter $'\mu'$ and $'\lambda'$ the p.d.f. $h(.)$ and c.d.f. $H(.)$.

$U_{(1)}$: a continuous random variable denoting the inter-arrival times between the contacts follows smallest order statistics with p.d.f. $f_{u_{(1)}}(t)$ and c.d.f. $F_{u_{(1)}}(t)$.

$g_k(.)$: the p.d.f. of the random variable $\sum_{i=1}^{k} X_i$

$F_k(.)$: the $'k'^{th}$ convolution of $F(.)$.

T : a continuous random variable denoting the time to seroconversion with p.d.f. $l(.)$ and c.d.f. $L(.)$.

$V_k(t)$: probability of exactly $'k'$ contacts in $(0,t]$.

$l^*(s)$: the Laplace Stieltjes transform of $l(t)$.

$f^*(s)$: the Laplace Stieltjes transform of $f(t)$.

Results

It can be shown that

$$P\left[\sum_{i=1}^{k} X_i < Y\right] = \int_0^{\infty} g_k(x)\,\overline{H}(x)\,dx$$

Let Y ~ Generalized Rayleigh Distribution (α, λ, μ)

$$\overline{H}(x) = 1 - \left[1 - e^{-\lambda(x-\mu)^2}\right] = e^{-\lambda(x-\mu)^2}$$

Hence

$$P\left[\sum_{i=1}^{k} X_i < Y\right] = \int_0^{\infty} g_k(x)\left[e^{-\lambda(x-\mu)^2}\right]$$

$$= \left[g^*\lambda(1-\mu)^2\right]^k$$

The survival function S(t) is

S(t) = P[T > t]

$$= \sum_{k=0}^{\infty} V_k(t)\, P\left[\sum_{i=1}^{k} X_i < Y\right]$$

$$= \sum_{k=0}^{\infty}\left[F_k(t) - F_{k+1}(t)\right]\left[g^*\lambda(1-\mu)^2\right]^k$$

$$= \sum_{k=0}^{\infty} \Pr\{\text{there are exactly k contacts in } (0,t]\}$$

* Pr{the cumulative total of antigenic diversity < Y}

L(t) = 1 - S(t)

$$= 1 - \left\{\sum_{k=0}^{\infty}\left[F_k(t) - F_{k+1}(t)\right]\left[g^*\lambda(1-\mu)^2\right]^k\right\}$$

$$L(t) = \left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]\sum_{k=1}^{\infty} F_k(t)\left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]^{k-1}$$

On simplification

$$l(t) = 2\left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]\sum_{k=1}^{\infty}\left[f_k(t)\right]\left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]^{k-1}$$

Now Taking Laplace Stieltjes transform of l(t),which is denoted by l*(s), we have

$$l^*(s) = \frac{\left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right] f^*(s)}{\left[1 - g^*\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right) f^*(s)\right]}$$

On simplification … (1)

The inter-arrival times $U_1, U_2, U_3, ..., U_k$ are i.i.d random variables. Now arranging $U_1, U_2, U_3, ..., U_k$ in the increasing order of magnitude we get

$$U_{(1)} \le U_{(2)} \le U_{(3)} \le ..... \le U_{(k)}.$$

The p.d.f of the smallest order statistics is

$$f_{u_{(1)}}(t) = K\left[1 - F(t)\right]^{k-1} f(t)$$

The Laplace Stieltjes transform the same is given by

$$f^{*}{}_{u_{(1)}}(t) = \int_0^{\infty} e^{-st} K\left[1 - F(t)\right]^{k-1} f(t)\,dt$$

Assuming that f(t) follows exp(c), it can be shown that

$$f^{*}{}_{u_{(1)}}(s) = \frac{kc}{kc + s} \qquad \ldots (2)$$

Substituting equation (2) in (1), we get

$$l^{*}(s) = \frac{\left[1 - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]kc}{\left[kc + s - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)kc\right]}$$

On Simplification

$$E(T) = -\left.\frac{dl^{*}s}{ds}\right|_{s=0}$$

$$= \frac{kc\left[1 - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]}{(kc)^2\left[kc + s - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]^2}$$

On Simplification

At s = 0

$$E(T) = \frac{1}{kc\left[1 - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]} \qquad \ldots (3)$$

Let $g^{*}(.) \square \exp(\alpha)$

$$g^{*}(\lambda) = \frac{\alpha}{\alpha + \lambda}, g^{*}2(\lambda\mu) = \frac{\alpha}{\alpha + 2\lambda\mu}, g^{*}(\lambda\mu^2) = \frac{\alpha}{\alpha + \lambda\mu^2} \qquad \ldots (4)$$

Then (4) in (3), we can get

$$E(T) = \frac{1}{kc\left[1 - \left\{\frac{\alpha}{\alpha + \lambda} + \frac{\alpha}{\alpha + \lambda\mu^2} - \frac{\alpha}{\alpha + 2\lambda\mu}\right\}\right]}$$

$$= \frac{1}{kc\left[1 - \left\{\frac{\alpha^3 + 4\alpha^2\lambda\mu + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu - \alpha\lambda^2\mu^2}{\left(\alpha^2 + 2\alpha\lambda\mu + \alpha\lambda + 2\lambda^2\mu\right)\left(\alpha + \lambda\mu^2\right)}\right\}\right]}$$

$$E[T] = \frac{\alpha^3 + \alpha^2\lambda + \alpha^2\lambda\mu^2 + 2\alpha^2\lambda\mu + \alpha\lambda^2\mu^2 + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu + 2\lambda^3\mu^3}{kc\lambda\left[\alpha^2 + \alpha^2\mu^2 - 2\alpha^2\mu + 2\alpha\lambda\mu^2 + 2\lambda^2\mu^3\right]}$$

On Simplification ….. (5)

$$E(T^2) = \left.\frac{d^2l^{*}s}{ds^2}\right|_{s=0}$$

$$= \frac{2kc\left[1 - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]}{\left[kc + s - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)kc\right]^3}$$

At s = 0

$$E\left[T^2\right] = \frac{2}{(kc)^2\left[1 - g^{*}\left(\lambda + \lambda\mu^2 - 2\lambda\mu\right)\right]^2} \qquad \ldots (6)$$

Let $g^{*}(.) \square \exp(\alpha)$

$$g^{*}(\lambda) = \frac{\alpha}{\alpha + \lambda}, g^{*}2(\lambda\mu) = \frac{\alpha}{\alpha + 2\lambda\mu}, g^{*}(\lambda\mu^2) = \frac{\alpha}{\alpha + \lambda\mu^2}$$

$$E(T^2) = \frac{2}{(kc)^2\left[1 - \left\{\frac{\alpha}{\alpha + \lambda} + \frac{\alpha}{\alpha + \lambda\mu^2} - \frac{\alpha}{\alpha + 2\lambda\mu}\right\}\right]^2}$$

$$E(T^2) = \frac{2\left(\begin{array}{c}\alpha^3 + \alpha^2\lambda + \alpha^2\lambda\mu^2 + 2\alpha^2\lambda\mu + \alpha\lambda^2\mu^2 \\ + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu + 2\lambda^3\mu^3\end{array}\right)^2}{(kc)^2\lambda^2\left(2\lambda^2\mu^3 + 2\alpha\lambda\mu^2 + \alpha^2 + \alpha^2\mu^2 - 2\alpha^2\mu\right)^2}$$

On Simplification

Hence, the variance of time to seroconversion is V(T) = E(T2) - [E(T)]2

$$V(T) = \frac{2\left(\begin{array}{c}\alpha^3 + \alpha^2\lambda + \alpha^2\lambda\mu^2 + 2\alpha^2\lambda\mu + \alpha\lambda^2\mu^2 \\ + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu + 2\lambda^3\mu^3\end{array}\right)^2}{(kc)^2\lambda^2\left(2\lambda^2\mu^3 + 2\alpha\lambda\mu^2 + \alpha^2 + \alpha^2\mu^2 - 2\alpha^2\mu\right)^2} - \left[\frac{\left(\begin{array}{c}\alpha^3 + \alpha^2\lambda + \alpha^2\lambda\mu^2 + 2\alpha^2\lambda\mu + \alpha\lambda^2\mu^2 \\ + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu + 2\lambda^3\mu^3\end{array}\right)}{(kc)\lambda\left(2\lambda^2\mu^3 + 2\alpha\lambda\mu^2 + \alpha^2 + \alpha^2\mu^2 - 2\alpha^2\mu\right)}\right]^2$$

$$V[T] = \frac{\left(\begin{array}{c}\alpha^3 + \alpha^2\lambda + \alpha^2\lambda\mu^2 + 2\alpha^2\lambda\mu + \alpha\lambda^2\mu^2 \\ + 2\alpha\lambda^2\mu^3 + 2\alpha\lambda^2\mu + 2\lambda^3\mu^3\end{array}\right)^2}{(kc)^2\lambda^2\left(2\lambda^2\mu^3 + 2\alpha\lambda\mu^2 + \alpha^2 + \alpha^2\mu^2 - 2\alpha^2\mu\right)^2}$$

On Simplification

Numerical Illustrations

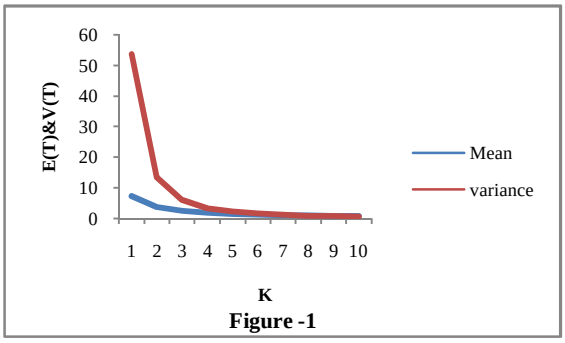

Figure -1

Table-1

k	$\mu=0.5,\alpha=0.2,\lambda=0.3$ $c=0.5$	
	Mean	**Variance**
1	7.333333	53.77778
2	3.666667	13.44444
3	2.444444	5.975309
4	1.833333	3.361111
5	1.466667	2.151111
6	1.222222	1.493827
7	1.047619	1.097506
8	0.916667	0.840278
9	0.814815	0.663923
10	0.733333	0.537778

Table 2

μ	$\alpha=0.2,\lambda=0.3,k=2$ $c=0.5$	
	Mean	**Variance**
0.5	3.666667	13.444444
1	2.222222	4.938272
1.5	1.807512	3.267099
2	1.666667	2.777778
2.5	1.609628	2.590903
3	1.584699	2.511272
3.5	1.573951	2.477323
4	1.570048	2.465052
4.5	1.569630	2.463737
5	1.571028	2.468128

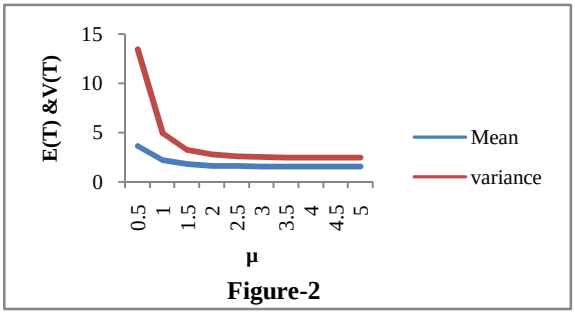

Figure-2

Table 3

λ	$\mu=0.5,\alpha=0.2,k=2$ $c=0.5$	
	Mean	**Variance**
0.5	2.600000	6.760000
1	1.800000	3.240000
1.5	1.533333	2.351111
2	1.400000	1.960000
2.5	1.320000	1.742400
3	1.266667	1.604444
3.5	1.228571	1.509388
4	1.200000	1.440000
4.5	1.177778	1.387160
5	1.160000	1.345600

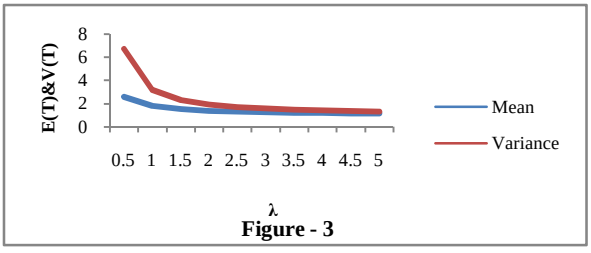

Figure - 3

Table 4

α	$\mu=0.2,\lambda=0.3,k=2$ $c=0.5$	
	Mean	**Variance**
0.1	2.333333	5.444444
0.2	3.666667	13.444444
0.3	5.000000	25.000000
0.4	6.333333	40.111111
0.5	7.666667	58.777778
0.6	9.000000	81.000000
0.7	10.333333	106.777778
0.8	11.666667	136.111111
0.9	13.000000	169.000000
1	14.333333	205.444444

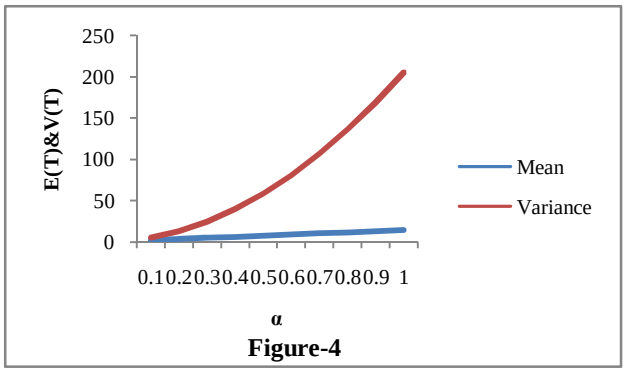

Figure-4

Table 5

c	$\mu=0.5,\alpha=0.2,\lambda=0.3$ $k=2$	
	Mean	**Variance**
1	1.833333	3.361111
2	0.916667	0.840278
3	0.611111	0.373457
4	0.458333	0.210069
5	0.366667	0.134444
6	0.305556	0.093364
7	0.261905	0.068594
8	0.229167	0.052517
9	0.203704	0.041495
10	0.183333	0.033611

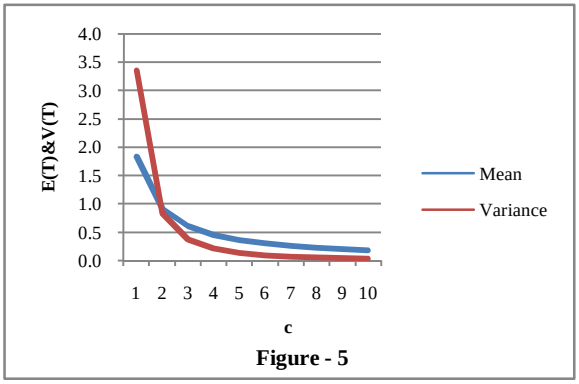

Figure - 5

CONCLUSIONS

1. At the value of k increases the mean time to seroconversion and its variance decreases. This is due to the fact that as k namely number of contacts in (0,t] decreases it means that the contact are more frequent.

Hence, it takes less time to cross the threshold. It is easily seen from Table (1) and Fig. (1).

2. From the fixed value of k, α, c and λ when threshold parameter μ is allowed to increase than the expected time to seroconversion and its variance time to seroconversion are decreases as indicated in Table (2) and Fig.(2).
3. From the fixed value of k, α, c and μ when threshold parameter λ is allowed to increase than the expected time to seroconversion and its variance time to seroconversion are decreases as indicated in Table (3) and Fig.(3).
4. It is observed from the Table (4), the contribution to the antigenic diversity threshold parameter 'α' which increases, then the mean time to seroconversion and its variance increases.
5. As the value of the parameter 'c' is the distribution of the times intervals between successive contacts shown an increase it means that the average time intervals between successive contacts which is given by $E(U) = \frac{1}{c}$ since U~ Exp(c), therefore time intervals between successive contacts becomes smaller and hence the mean time to seroconversion and its variance decreases.

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