Vol.5.Issue.1.2017 (Jan.-Mar)

BULLETIN OF MATHEMATICS AND STATISTICS RESEARCH

A Peer Reviewed International Research Journal

http://www.bomsr.com
Email:editorbomsr@gmail.com

RESEARCH ARTICLE

ISSN:2348-0580

A STOCHASTIC APPROACH TO DETERMINE THE EXPECTED TIME TO CROSS THE ANTIGENIC DIVERSITY THRESHOLD WHEN INTERCONTACT TIME FORM A GEOMETRIC PROCESS

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ISSN:2348-0580
BOMSR
BULLETIN OF MATHEMATICS AND STATISTICS RESEARCH
www.bomsr.com

ABSTRACT

This paper focuses on the study of a stochastic model for predicting the expected time to cross the antigenic diversity threshold of HIV infected using geometric process. In the estimation of expected time to cross the antigenic diversity threshold of HIV infected, there is an important role for the inter-arrival time between successive contact and it has the significant influence. We propose a stochastic model assuming the inter-contact time between successive contacts forms a geometric process and threshold distribution is exponential-geometric distribution. The mean time to seroconversion and its variance are derived and numerical illustrations are provided.

Key words: Human Immuno Deficiency Virus (HIV), Geometric process, Acquired Immuno Deficiency Syndrome (AIDS), Antigenic Diversity Threshold, Seroconversion. Inter contact time.

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1. INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a lentivirus that causes HIV infection and over time Acquired Immuno Deficiency Syndrome (AIDS). AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, preejaculate, or breast milk. Within these bodily fluids, HIV present as both free virus particles and virus within infected immune cells.

The time to seroconversion from the point of infection depends upon what is known as antigenic diversity which acts against the immune ability of an individual. Every individual has a threshold level of antigenic diversity. If the antigenic diversity due to acquiring more and more of HIV infection due to homo or heterosexual contacts exceeds the threshold level, then the immune system of the human body is completely suppressed which in turn leads to seroconversion. For a

detailed study of antigenic diversity threshold and its estimation one can refer to Nowak and May (1991) and Stilianakis et al. (1994).

A stochastic model based on the cumulative damage process has been derived by Sathiyamoorthi and Kannan (2001) and using this model it is possible to obtain the expected time to seroconversion and its variance. Every contact is depicted as a shock and in every contact there is some contribution to antigenic diversity which is otherwords is the damage to the immune capacity of an individual. Cumulative damage process and shock model are widely known in reliability theory. A detailed account of the same could be seen in Esary et al. (1973). In developing such a model the basic assumption made was that the inter contact timing between successive contact are i.i.d random variable. In this paper it is assumed that the sequence of the random variable denoting the inter-arrival time between contact to be a geometric process. A person who is exposed to a contact/ transmission, because mentally alert and postponed the next contact. After the second contact the fear is still increase and the time interval between second and third contact is further elongated and so on. Therefore the successive time interval forms a geometric process.

For detailed study of geometric process and its property one can refer to Lam Yeh (1988). A stochastic model for the estimation of expected time to seroconversion of HIV infected using geometric process has been derived under different threshold distribution (Gamma, Mixed Exponential, Exponentiated Exponential) by Kannan et al. (2008,2012 and 2013). In this paper a stochastic model to determine the expected time to cross the antigenic diversity threshold and its variance is discussed under the assumption that, time interval between successive contacts are distributed as a geometric processes using Exponential-geometric distribution as a threshold. In this study the theoretical results are substantiated by using numerical data simulated.

2. ASSUMPTIONS OF THE MODEL

(i) The transmission of HIV only through sexual contacts.

(ii) An uninfected individual has sexual contacts with a HIV infected partner and in every contact a random number of HIV are transmitted.

(iii) The inter-arrival times between successive contacts are random variables which forms a geometric process.

(iv) The sequence of successive contacts and threshold level are independent.

(v) If the total damage caused when crosses a threshold level which itself a random variable, the seroconversion occurs and a person is recognized as a seropositive.

3. NOTATIONS

X_i : A random variable denoting the increase in the antigenic diversity arising due to the HIV transmitted during the i^{th} contact X_1, X_2,…, X_k are continuous i.i.d. random variables, with p.d.f. g(.) and c.d.f. G(.).

Y : A random variable representing antigenic diversity threshold and follows exponential-geometric distribution with parameters β and p, the p.d.f. being h(.) and c.d.f. H(.).

U_i : A continuous random variable denoting the inter-arrival times between successive contacts with p.d.f *f*(.) and c.d.f F(.).

$g_k(.)$: 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).

4. RESULTS

The survival function S (t) is

$$S(t) = P(T > t)$$

$$= \sum_{k=0}^{\infty} Pr\{there\ are\ exactly\ k\ contacts\ in\ (0,t]\} \times Pr\{the\ cumulative\ total\ of\ antigenic\ diversity < Y\}$$

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

It can be shown that,

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

Where, $\bar{H}(x) = 1 - H(x)$

The probability density function of exponential-geometric distribution is,

$$h(y) = \beta(1-p)\, e^{-\beta y}(1 - pe^{-\beta y})^2$$

and its distribution function is

$$H(y) = \left(1 - e^{-\beta y}\right)(1 - pe^{-\beta y})^{-1}$$

And

$$\bar{H}(y) = \frac{e^{-\beta y}(1-p)}{(1-pe^{-\beta y})}$$

Since Y is taken to be exponential-geometric distribution (β, p).

Hence

$$P\left[\sum_{i=1}^{k} X_i < y\right] = \theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta + i\beta}\right] \quad \ldots(2)$$

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

$$S(t) = \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\left[\theta(-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta + i\beta}\right]\right]$$

L(t) = 1 – S(t)

$$= 1 - \left\{\sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta + i\beta}\right]\right]\right\}$$

$$l(t) = -\sum_{k=0}^{\infty}[f_k^*(t) - f_{k+1}^*(t)]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta + i\beta}\right]\right]$$

Taking Laplace transform of l(t) is,

$$l^*(s) = -\sum_{k=0}^{\infty}[f_k^*(s) - f_{k+1}^*(s)]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta + i\beta}\right]\right] \quad \ldots(3)$$

Where $f^*(s)$ is the Laplace transform of f (.).

Since U_i's form geometric process $f_k^*(s)$ and $f_{k+1}^*(s)$ can be written as

$$f_k^*(s) = \prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right) f_{k+1}^*(s) \quad \text{and} \quad f_{k+1}^*(s) = \prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right) \quad \ldots(4)$$

Substitute (4) in (3), we get,

$$l^*(s) = -\sum_{k=0}^{\infty}\left[\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right) - \prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]$$

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

$$= \sum_{k=0}^{\infty}\left[\left.\frac{d}{ds}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0} - \left.\frac{d}{ds}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0}\right]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right] \quad \ldots(5)$$

Consider,

$$\left.\frac{d}{ds}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0}$$

$$= \left.\frac{d}{ds}\left\{f^*(s)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a^2}\right)\ldots..f^*\left(\frac{s}{a^{k-1}}\right)\right\}\right|_{s=0}$$

$$= f^{*\prime}(0) + \frac{1}{a}f^{*\prime}(0) + \frac{1}{a^2}f^{*\prime}(0) + \cdots + \frac{1}{a^{k-1}}f^{*\prime}(0)$$

$$\left.\frac{d}{ds}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0} = f^{*\prime}(0)\left[\frac{a^k-1}{(a-1)a^{k-1}}\right] \quad \ldots(6)$$

Again consider,

$$\left.\frac{d}{ds}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0}$$

$$= \left.\frac{d}{ds}\left\{f^*(s)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a^2}\right)\ldots..f^*\left(\frac{s}{a^{k-1}}\right)f^*\left(\frac{s}{a^k}\right)\right\}\right|_{s=0}$$

$$= f^{*\prime}(0) + \frac{1}{a}f^{*\prime}(0) + \frac{1}{a^2}f^{*\prime}(0) + \cdots + \frac{1}{a^{k-1}}f^{*\prime}(0) + \frac{1}{a^k}f^{*\prime}(0)$$

$$\left.\frac{d}{ds}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\right|_{s=0} = f^{*\prime}(0)\left[\frac{a^{k+1}-1}{(a-1)a^k}\right] \quad \ldots(7)$$

Substitute equation (6) and (7) in (5) we get,

$$E(T) = \left[f^{*\prime}(0)\left[\frac{a^k-1}{(a-1)a^{k-1}}\right] - f^{*\prime}(0)\left[\frac{a^{k+1}-1}{(a-1)a^k}\right]\right]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]$$

$$= f^{*\prime}(0)\left[\frac{a^{k+1}-a-a^{k+1}+1}{(a-1)a^k}\right]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]$$

$$= -f^{*\prime}(0)\left[\frac{1}{a^k}\right]\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right] \quad \ldots(8)$$

Let f(.)~ Exponential with parameter μ, then,

$$f^*(\mathrm{s}) = \frac{\mu}{\mu+\mathrm{s}}\ , \qquad f^{*\prime}(0) = -\frac{1}{\mu} \quad , \quad and \quad f^{*\prime\prime}(0) = \frac{2}{\mu^2} \quad \ldots(9)$$

Substitute equation (9) in (8), we get,

$$E(T) = -\frac{dl^*(s)}{ds}\Big|_{s=0} = \frac{1}{a^k\mu}\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right] \quad \ldots(10)$$

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

$$= -\sum_{k=0}^{\infty}\left[\frac{d^2}{ds^2}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0} - \frac{d^2}{ds^2}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0}\right] \times\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2 \quad \ldots(11)$$

Consider,

$$\frac{d^2}{ds^2}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0}$$

$$= \frac{d^2}{ds^2}\left\{f^*(s)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a^2}\right)\ldots\ldots f^*\left(\frac{s}{a^{k-1}}\right)\right\}\Big|_{s=0}$$

$$= f^{*\prime\prime}(0)\frac{a^{2k}-1}{(a^2-1)a^{2(k-1)}} - \left[f^{*\prime}(0)\right]^2\frac{a^{2k}-1}{(a^2-1)a^{2(k-1)}} + \left[f^{*\prime}(0)\right]^2\frac{a^{2k}-2a^k+1}{(a-1)^2a^{2(k-1)}}$$

On simplification we get,

$$\frac{d^2}{ds^2}\left(\prod_{n=1}^{k} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0} = \left[f^{*\prime\prime}(0) - \left[f^{*\prime}(0)\right]^2\right]\frac{a^{2k}-1}{(a^2-1)a^{2(k-1)}} + \left[f^{*\prime}(0)\right]^2\frac{a^{2k}-2a^k+1}{(a-1)^2a^{2(k-1)}} \quad \ldots(12)$$

Again consider,

$$\frac{d^2}{ds^2}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0}$$

$$= \frac{d^2}{ds^2}\left\{f^*(s)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a}\right)f^*\left(\frac{s}{a^2}\right)\ldots\ldots f^*\left(\frac{s}{a^{k-1}}\right)f^*\left(\frac{s}{a^k}\right)\right\}\Big|_{s=0}$$

$$= f^{*\prime\prime}(0)\frac{a^{2(k+1)}-1}{(a^2-1)a^{2(k)}} - \left[f^{*\prime}(0)\right]^2\frac{a^{2(k+1)}-1}{(a^2-1)a^{2(k)}} + \left[f^{*\prime}(0)\right]^2\frac{a^{2(k+1)}-2a^{(k+1)}+1}{(a-1)^2a^{2(k)}}$$

On simplification we get,

$$\frac{d^2}{ds^2}\left(\prod_{n=1}^{k+1} f^*\left(\frac{s}{a^{n-1}}\right)\right)\Big|_{s=0} = \left[f^{*\prime\prime}(0) - \left[f^{*\prime}(0)\right]^2\right]\frac{a^{2(k+1)}-1}{(a^2-1)a^{2(k)}} + \left[f^{*\prime}(0)\right]^2\frac{a^{2(k+1)}-2a^{(k+1)}+1}{(a-1)^2a^{2(k)}} \quad \ldots(13)$$

Substitute equation (12) and (13) in equation (11), we get,

$$= -\left\{\left[\left[f^{*''}(0) - \left[f^{*'}(0)\right]^2\right]\left(\frac{a^{2k}-1}{(a^2-1)a^{2(k-1)}} - \frac{a^{2(k+1)}-1}{(a^2-1)a^{2(k)}}\right)\right.\right.$$
$$\left.\left. + \left[f^{*'}(0)\right]^2\left(\frac{a^{2k}-2a^k+1}{(a-1)^2a^{2(k-1)}} - \frac{a^{2(k+1)}-2a^{(k+1)}+1}{(a-1)^2a^{2(k)}}\right)\right]\right.$$
$$\left. \times \left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2\right\}$$

Using equation (9), we get,

$$= -\left\{\left[\left[\frac{2}{\mu^2} - \frac{1}{\mu^2}\right]\left(\frac{a^{2k}-1}{(a^2-1)a^{2(k-1)}} - \frac{a^{2(k+1)}-1}{(a^2-1)a^{2(k)}}\right)\right.\right.$$
$$\left.\left. + \left[\frac{1}{\mu^2}\right]\left(\frac{a^{2k}-2a^k+1}{(a-1)^2a^{2(k-1)}} - \frac{a^{2(k+1)}-2a^{(k+1)}+1}{(a-1)^2a^{2(k)}}\right)\right]\right.$$
$$\left. \times \left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2\right\}$$

$$E(T^2) = \left.\frac{d^2 l^*(s)}{ds^2}\right|_{s=0} = \frac{2}{a^{2k}\mu^2}\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2 \quad \ldots(14)$$

Hence ,

$$V(T) = E(T^2) - [E(T)]^2 \quad \ldots(15)$$
$$= \frac{2}{a^{2k}\mu^2}\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2 - \frac{1}{a^k\mu}\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2$$
$$V(T) = \frac{1}{a^{2k}\mu^2}\left[\theta(1-p)\sum_{i=1}^{k}\left[\frac{p^{i-1}}{\theta+i\beta}\right]\right]^2 \quad \ldots(16)$$

(On simplification)

5. NUMERICAL ILLUSTRATIONS

Table -1

a	$\theta = 0.2, p = 0.5,$ $k = 1, \mu = 1, \beta = 0.4$	
	E(T)	V(T)
1	0.142857	0.020408
2	0.071429	0.005102
3	0.047619	0.002267
4	0.035714	0.001275
5	0.028571	0.000816
6	0.023810	0.000566
7	0.020408	0.000416
8	0.017857	0.000318
9	0.015873	0.000251
10	0.014286	0.000204

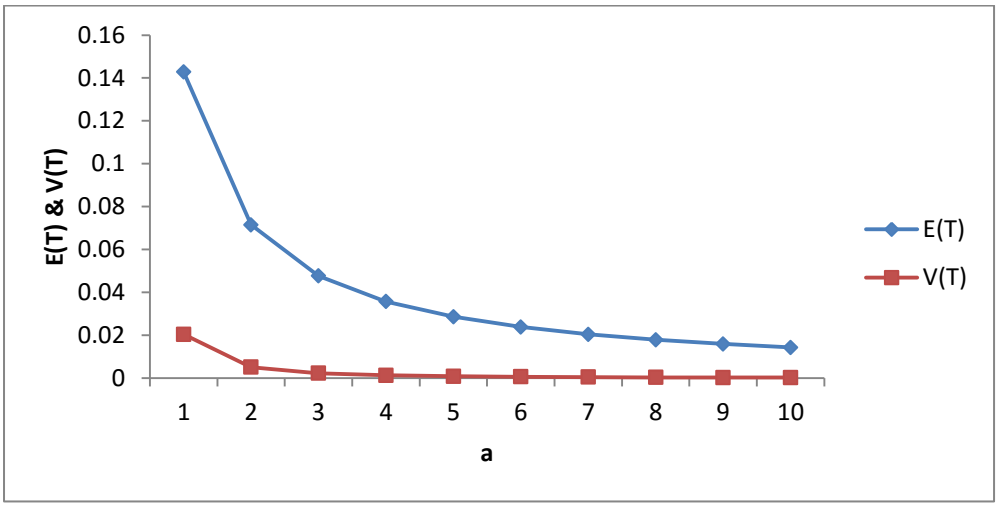

Figure -1

Table -2

μ	$\theta = 0.1, p = 0.5,$ $k = 2, a = 2, \beta = 0.7$	
	E(T)	V(T)
1	0.208333	0.043402
2	0.052083	0.002712
3	0.017361	0.000300
4	0.006510	4.24E-05
5	0.002604	6.78E-06
6	0.001085	1.18E-06
7	0.000465	2.16E-07
8	0.000203	4.14E-08
9	9.04E-05	8.18E-09
10	4.07E-05	1.66E-09

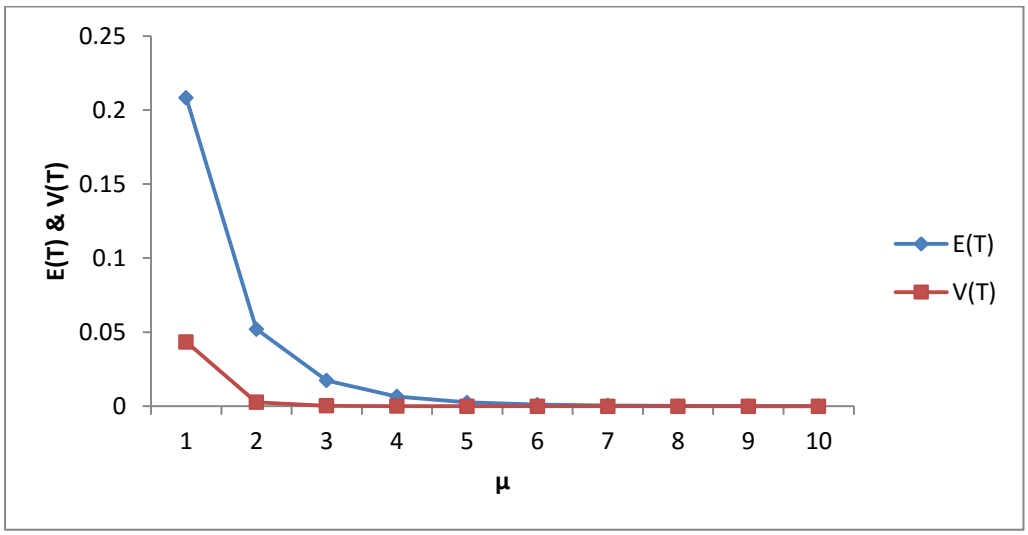

Figure -2

Table -3

θ	$\beta = 0.6, k = 1,$ $\mu = 1, a = 2, p = 0.5$	
	E(T)	V(T)
0.1	0.041667	0.001736
0.2	0.071429	0.005102
0.3	0.093750	0.008789
0.4	0.111111	0.012345
0.5	0.125000	0.015625
0.6	0.136364	0.018595
0.7	0.145833	0.021267
0.8	0.153846	0.023668
0.9	0.160714	0.025829
1.0	0.166667	0.027777

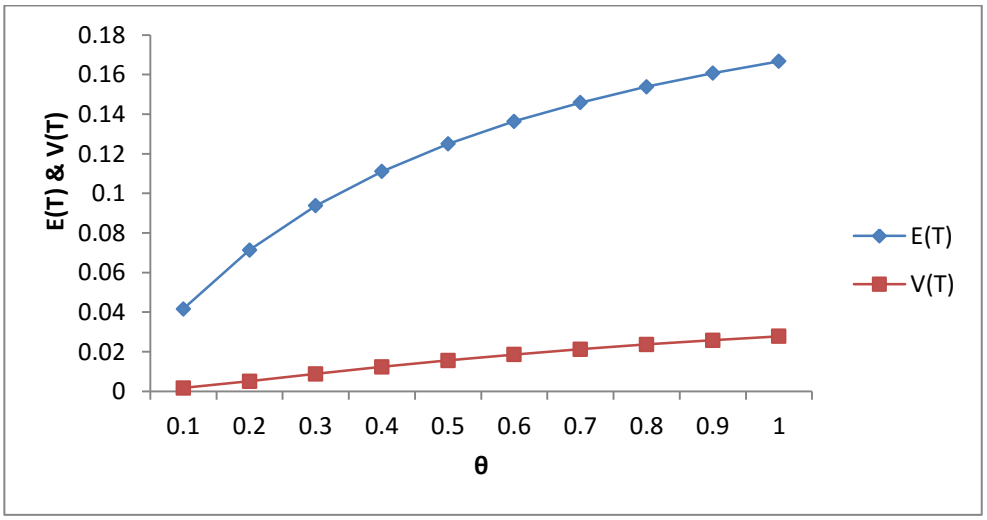

Figure -3

Table -4

p	$\theta = 0.3, a = 2,$ $\mu = 1, k = 1, \beta = 0.8$	
	E(T)	V(T)
0.1	0.337500	0.113906
0.2	0.240000	0.057600
0.3	0.175000	0.030625
0.4	0.128571	0.016530
0.5	0.093750	0.008789
0.6	0.066667	0.004444
0.7	0.045000	0.002025
0.8	0.027273	0.000743
0.9	0.012500	0.000156

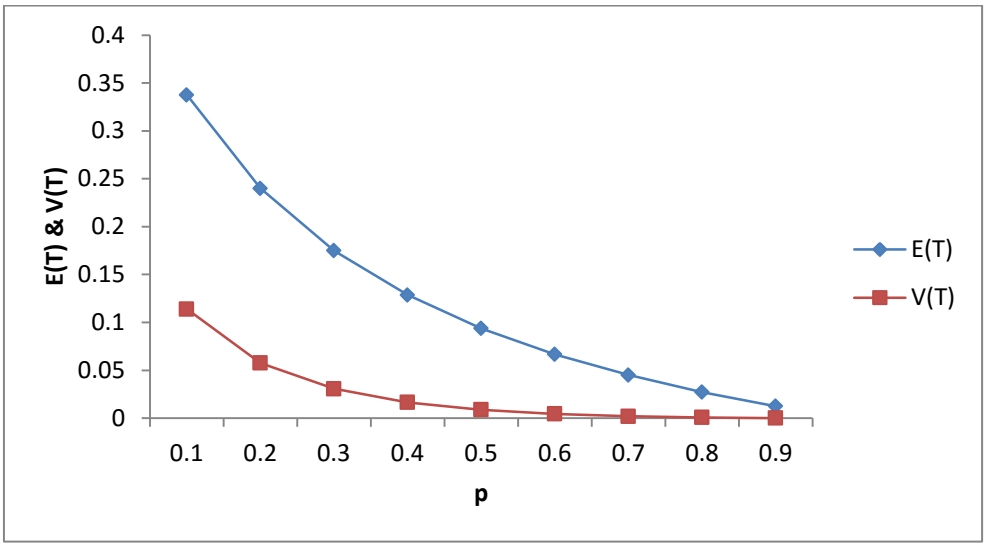

Figure -4

Table -5

β	$\theta = 0.4, a = 2,$ $\mu = 1, k = 1, p = 0.2$	
	E(T)	V(T)
0.1	0.266667	0.071111
0.2	0.053333	0.002844
0.3	0.010667	0.000114
0.4	0.002133	4.55E-06
0.5	0.000427	1.82E-07
0.6	8.53E-05	7.28E-09
0.7	1.71E-05	2.91E-10
0.8	3.41E-06	1.17E-11
0.9	6.83E-07	4.66E-13
1.0	1.37E-07	1.86E-14

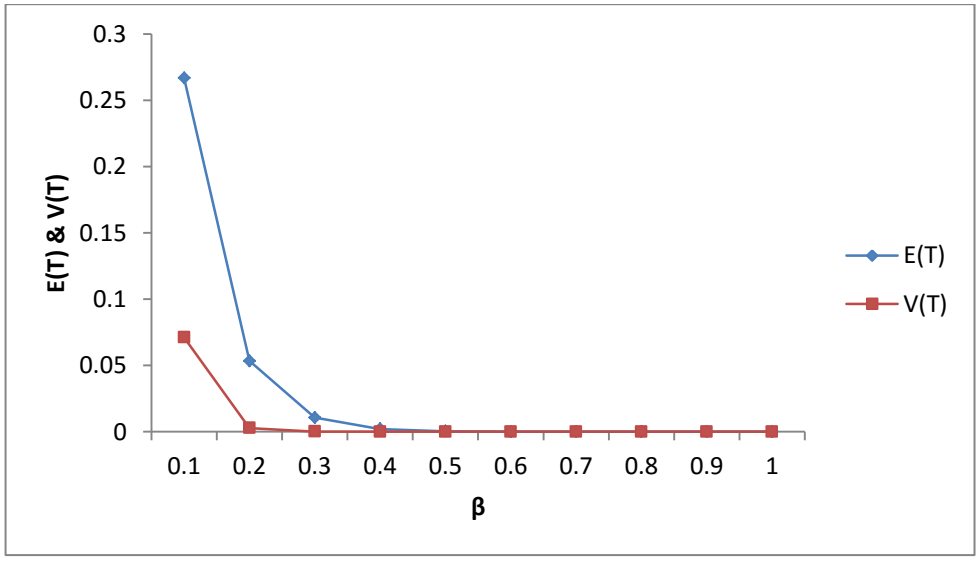

Figure -5

6. CONCLUSIONS

It can be seen from Table-1, that as 'a' increases then the expected time to seroconversion decreases. This is due to the fact that in a geometric process if a > 1, then the sequence of random variables would be decreasing and so the interval time forms a decreasing sequence. Hence expected time to seroconversion decreases by the fact that the contact would be more frequent. Similarly the variance of seroconversion time also decreases.

From the Table 2, the value of μ namely the parameter of the random variable denoting inter-arrival time between contacts increases then the expected time to seroconversion decreases and also variance time to seroconversion decreases.

As the value of θ, which is namely, the parameter of the random variable X_i denoting contribution to the antigenic diversity increases, then the expected time to seroconversion and variance time to seroconversion both increases, as indicated in Table 3 and Figure 3.This is due to fact that g(.) is the distribution of $X_{(i)}$, the magnitude of contribution to antigenic diversity. Since $E(X) = \frac{1}{\theta}$, as θ increases there is a decrease in the contribution of antigenic diversity.

From the Table 4, the behavior of E(T) for fixed parameters when p is allowed to increase then mean time to seroconversion decreases. The same tendency is also noted on the variance of the seroconversion time of the HIV transmission.

It is observed from the Table 5 and also the graph as the value of β which is the parameter of the exponential-geometric distribution of the threshold increases the mean time to seroconversion decreases. It is also quite reasonable as regard the variation it could be seen that as the value of β increases, the variance decreases.

ACKNOWLEDGEMENT

We are immensely grateful to Dr.R.sathiyamoorthi, former Professor and Head, Department of Statistics, Annnamalai University, Chidambaram and Dr.G.S.Harisekharan, WIPRO, Chennai for their invaluable constructive suggestions, guidance and intellectual support.

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