ESTIMATION OF THE LIKELY TIME FOR SEROCONVERSION IN HIV INFECTION

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ABSTRACT

*T*he acronym AIDS was coined to describe an Acquired Immune Deficiency Syndrome. The causative agent of this disease is human retrovirus – Human Immunodeficiency Virus. AIDS is a chronic, life-threatening condition caused by the HIV. As a retrovirus HIV shows a high replication error rate and leads to the creation of distinct viral genomes with different immunological properties. This character of HIV is called antigenic diversity. Thus, due to the ongoing antigenic variation more and more mutant specific immune responses become activated. It is well known that the HIV transmission occurs through various modes and the most important, widely prevalent mode of transmission is the homo or hetro sexual contacts. On the successive occasion of contact with one or more infected partners, the transmission of more number of HIV is facilitated, which in turn contributes to the increase in antigenic diversity of HIV. The antigenic diversity threshold is a particular level of the antigenic diversity, above which the immune system is unable to suppress the viral population. According to Stilianakis 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 leads to the onset of AIDS symptoms in an infected person. HIV infection and its spread is a serious problem affecting not only the social life of the people but also the economy of the country itself. The progression of HIV is mainly due to what is called the antigenic diversity of the antigen which is HIV. If the antigenic diversity crosses the threshold level then the seroconversion will take place. In this paper two different models are discussed. In model 1, a Stochastic model is discussed for the purpose of estimating the time to seroconversion of the HIV infected. In model 2, a stochastic model is developed under the assumption that the threshold level which is a random variable undergoes a parametric change after crossing a truncation point. The expected time to seroconversion is estimated and its variance is also found out using the Shock model and cumulative damage concept.

Keywords used: HIV Infection, Antigenic Diversity Threshold (ADT), Antigenic Diversity, Immune System, Acquired Immune Deficiency Syndrome, Seroconversion, Expected Time to Seroconversion, Shock Model and Cumulative Damage Process.

INTRODUCTION:

The acronym AIDS was coined to describe an Acquired Immune Deficiency Syndrome. The causative agent of this disease is a human retrovirus – Human Immunodeficiency Virus (HIV). The AIDS virus swept across the world, silently, before we even knew it existed. The world wide epidemic was well under way by 1981, when AIDS was first recognized and was given in name. The AIDS is a fatal illness caused by a retrovirus known as the HIV which breaks down the body's immune system, leaving the victim vulnerable to a host of life threatening opportunistic infections, neurological disorders, or unusual malignancies, among the special features of HIV infection are that once infected, it is probable that a person will be infected for life, strictly speaking, the term AIDS refer only to the last stage of the HIV infection. AIDS can be called our modern pandemic affecting both industrialized and developing countries. HIV impairs the human immune system and this makes its victims suffer from a variety of other infections and neoplasm's. On entering the human host HIV prefers certain cells which play a crucial role in the immune system. The core of virus, on entering the host's cell, investigates with the cellular DNA. When the host's cell replicates its DNA, the viral DNA is also replicated and large quantities of virus particles are produced. In the process the host cell is destroyed. HIV has been isolated from T_4 lymphocytes and monocytes obtained from blood and various organs of HIV infected person. When the virus (HIV) enters the body, the condition is described as HIV infection. At this stage, the persons may appear absolutely normal and may not be aware that this virus is present in his body. But when he is infected with various opportunistic infections, as a result of the immune deficiency caused by HIV, he is diagnosed as suffering from AIDS. The normal human immune system consists of phagocytes and macrophages and two kinds of lymphocytes called T and B cells which protect our body from infections. Whenever any unwanted substance, living or inert enters

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the body, the macrophage tries to engulf and digest the debris and summons helper T cells to the site. Helper T cell also identifies the enemy and messages go to the spleen and lymph nodes to produce more T cells to fight the infection. Activated by helper T cells, killer T cells specialize in killing the cells of the body that have been invaded by foreign organisms. B cells produce antibodies while the suppressor T cell plays a vital role in calling off the attack after the infection has been conquered. The AIDS virus invades and kills the helper T cells, there by short-circuiting the entire immune response. There is a spike protein on the surface of HIV which attaches to certain receptors (CD_4) on cells and hence the virus may infect all cells bearing CD_4, principally the T_4 (helper/inducer) lymphocytes in which the virus induces a lytic infection. The alveolar macrophages in the lung, langerhans cells in the dermis of skin and glial cells and microglia in the central nervous systems are all susceptible to infection by HIV. Smoking and alcohol consumption, together from deadly combination which may be responsible for weakening the immune system and increasing the susceptibility for various diseases including AIDS.

The problem of dealing with the spread of HIV epidemic is worldwide and a cure against for this infection seems to be very difficult. The HIV infection and spread is very subtle and the sero conversion of the infected is an important event. Once after this sero conversion the manifestation of AIDS symptoms occurs. In this process the antigenic diversity of the invading HIV antigens plays an important role. After infection the antigens in the process of reproduction adopt vary many strategies so that the newly formed antigens show a lot of changes in their invasion as well as their immune properties, with the result the immune system of the human body namely the antibodies generated by the human body are unable to fight against this antigens. This is because of the antigenic diversity. The rate of antigenic diversity has been mathematically found out by Novak and May. The estimation of infectivity has been studied by Shiboski and Jewell. An interesting problem of statistical study is to find out the likely time at which the antigenic diversity threshold will be crossed with the result that the collapse of the immune system will take place so that the sero conversion occurs. Many mathematical models have been developed by various authors. It is proposed to derive a mathematical model to determine the expected time to cross the antigenic diversity threshold. Also a stochastic model to estimate the expected time to sero conversion is discussed using the threshold distribution as one which satisfies so the called Setting the Clock Back to Zero (SCBZ) property. This property has been discussed by Raja Rao and Talwalker (1990). In the determination of the expected time to sero conversion, the shock model and cumulative damage process due to Esarry, Marshall and Proschan (1973) is used.

SHOCK MODELS AND CUMULATIVE DAMAGE PROCESS:

The shock models deal with the life distribution of devices or components, which are subjected to shocks. For example, the devices like on electric bulb, T.V picture tube etc., are subjected to random fluctuations in the voltage of electricity. A sequence of shocks occurs randomly in time and the instantaneous damage occurring at the random epochs cumulate to an unknown threshold value beyond which the system fails. The threshold level is itself a random variable. At every shock a random amount of damage is caused to the device and the damages in successive shocks get added together in the form of a cumulative damage. The rate at which the threshold is approached is also studied.

There are various approaches to the rate of accumulation of damage, but they all appear to be resolvable in terms of a stochastic process. If the damages caused by successive shocks are i.i.d random variables denoted as X_i, i = 1,2,3…n with common distribution function F (.) and the random threshold level Y is a random variable with distribution function G (.), then the probability that the device survives k damages is denoted as

$$P_k(X) = \int_0^\infty F_k(X)\, dG(X), \quad k = 1,2,...,$$

Where $F_k(X)$ is the k fold convolution F(X) with itself and $F_0(X) = 1$. The reliability R(t) of the device is given by

$$R(t) = \sum_{k=0}^\infty P_k\, V_k(t)$$

where $V_k(t)$ is the probability that k damages are caused during (0, t]. The above model has been considered by Esary, Marshall and Proschan (1973) with the underlying process generating the shocks as Poisson.

SETTING THE CLOCK BACK TO ZERO PROPERTY (SCBZ):

This concept has been recently developed by Raja Rao and Talwalker (1990). Let us assume that the distribution of the random variable X is given as f(x). We define the SCBZ property, as under:

Let x_0 be a truncation point and x be fixed. If

$$X \sim f(x,\theta_1) \qquad \text{when } X \le x_0$$
$$X \sim f(x, \theta_2) \qquad \text{when } X > x_0$$

then there is a parametric change in the distribution of the random variable x. The random variable x is said to satisfy the SCBZ property if

$$\frac{S(x + x_0, \theta_1, \theta_2)}{S(x_0, \theta_1)} = S(x, \theta_2)$$

where S(x, θ) is the survivor function.

i.e., S(x,θ)=1-F(x,θ) where F(x, θ) is the c.d.f of x.

It may be observed that in many of the real life situations the demand function may under go parametric changes due to the environmental, market and other economic considerations; taking this into account and incorporating the demand functions satisfying the SCBZ property, the model can be made more precise and accurate.

CHANGE OF DISTRIBUTION AT A CHANGE POINT:

The SCBZ property is one in which a random variable x has a parametric change after a certain value of x, say x_0, which is called the truncation point. It is also likely that on some occasions where the random variable x has a p.d.f f(x) with cdf F(x) if $X \leq x_0$ and after that it has the p.d.f h(x) with c.d.f H(x). Here x_0 is called the change point. The concept of change of distribution is discussed in Stagnl (1995). Suresh kumar (2006) has used this concept in shock model and cumulative damage process, to estimate the expected time to cross the threshold, where the threshold random variable Y undergoes a change in the distribution itself. In inventory theory, the probabilistic demand can undergo change in the very distribution itself after a change point. This concept is used in manpower planning problems.

ASSUMPTIONS:

1. Over a period of time a person has a number of sexual contacts with infected partners and as the time t.
2. Every contact contributes to the transmission of some HIV which in turn contribute of the increase of antigenic diversity.
3. A random amount of damage is caused to the immune capacity during every contact because of the antigenic diversity produced.
4. The antigenic diversity threshold of any individual is a random variable.
5. The inter arrival times between successive contacts are i.i.d random variables.
6. There is transmission of HIV in successive sexual contacts between the infected and uninfected.
7. There is contribution of antigenic diversity of HIV due to successive contacts.
8. The breakdown of the immune system occurs as and when the total antigenic diversity accumulation crosses the threshold level.
9. The intercontact times are random variables which are i.i.d.
10. The random amount of contribution to antigenic diversity and the threshold are independent.

NOTATIONS:

X_i: a random variable denoting the amount of contribution to antigenic diversity due to the HIV transmitted in the i1h contact.

f (.): The p.d.f of X_i

Y: random variable denoting the immune capacity level equivalent to the antigenic diversity threshold and y has p. d. f h(.) and c. d. f H (.).

T: a random variable denoting the time to CADT.

U_i: the random variable denoting the interarrival times between contacts and U_i has p. d. f f(.) and c. d. f. F(.)

$g^*(.)$: is the Laplace transform of g(.)

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

$F_k(.)$: k convolution of F(.)

g(.) : the p. d. f of antigenic diversity threshold.

It is assumed that the immune capacity of an individual is inversely proportional to the increasing antigenic diversity due to successive contacts. It is assumed that the hazard rate increases with time. The immune capacity decreases proportionately.

Immune capacity = I/Hazard rate = a+ b/t

where a and b are positive constants and t is positive time is postulated.

Now,

Hazard rate

$$h(t) = g(t) = \frac{g(t)}{1 - G(t)} = \frac{t}{at + b}$$

$$G(t) = \int_0^\infty \frac{t}{at + b} dt + \log c$$

Then

$$\int_0^\infty \frac{t}{at + b} dt = \frac{1}{a^2} In [x^{-b} e^x]$$

Therefore

$$- In [1 - G(t)] = In \left(x^{-b/a^2} e^{-x/a^2} \right) +$$

$$In (C) [1 - G(0)] = 1$$

Hence

$$C = \left(\frac{e}{b} \right)^{b/a^2}$$

$$1 - G(t) = \left(\frac{e}{b} \right)^{b/a^2} (at + b) e^{-(at+b)/a^2}$$

$$G(t) = 1 - \left[1 + \frac{at}{b} \right]^{b/a^2} e^{-t/a}$$

The probability density function of t is given by

$$g(t) = \frac{t}{b} \left[1 + \frac{at}{b} \right]^{(b/a^2)-1} e^{-t/a}$$

RESULTS:

MODEL 1:

The probability that the antigenic diversity developed by a single sexual contact does not cross the threshold level is given by

$$P[x < y] = \int_0^\infty F(x) g(x) dx$$

Therefore

Now, if we assume that the antigenic diversity induced by a single contact follows exponential distribution with mean β, then we have

$$F(x) = 1 - e^{(-1/\beta)x}$$

$$g(x) = \frac{x}{b}\left[1+\frac{ax}{b}\right]^{(b/a^2)-1} e^{-x/a}$$

Therefore,

$$P[x < y] = \int_0^\infty (1-e^{(-1/\beta)x}) e^{-x/a} \frac{x}{b}\left(1+\frac{ax}{b}\right)^{(b/a^2)-1} dx$$

$$= \int_0^\infty e^{-x/a} \frac{x}{b}\left(1+\frac{ax}{b}\right)^{b/a^2-1} dx - \int_0^\infty e^{-x\left(\frac{1}{\beta}+\frac{1}{a}\right)} \frac{x}{b}\left(1+\frac{ax}{b}\right)^{b/a^2-1} dx$$

assuming that $b = a^2$ on simplification it can be shown that

$$P[x < y] = 1 - \frac{\beta^2}{(\beta+a)^2}$$

$$= \frac{(\beta+a)^2 - \beta^2}{(\beta+a)^2}$$

$$P[X < Y] = \frac{a(a+2\beta)}{(\beta+a)^2}$$

$$P[X < Y] = \frac{a(a+2\beta)}{(\beta+a)^2} = A \ (say)$$

when there are K contacts we have

$$P[x_1 + x_2 + \ldots + x_k < Y] = A^k$$

Now the probability that the total antigenic diversity has not crossed the threshold level before the time t is given by

$$P[T > t] = \sum_{k=0}^\infty \Pr\{\text{there are exactly k contacts in } (0, t)\}$$
$$^* \Pr\{\text{the threshold is not crossed}\}$$

$$= \sum_{k=0}^\infty \frac{e^{-\lambda t}(\lambda t)^k}{k!} P[x_1 + x_2 + \ldots + x_k < Y]$$

$$= \sum_{k=0}^\infty \frac{e^{-\lambda t}(\lambda t)^k}{k!} A^k$$

The c. d. f. of the time to cross the antigenic diversity threshold is given by

$$H(t) = P[T \le t] = 1 - \sum_{k=0}^\infty \frac{e^{-\lambda t}}{k!} A^k$$

Take

$$B = A(\lambda t)$$

Therefore,

$$H(t) = 1 - e^{-\lambda t} \sum_{k=0}^\infty \frac{(B)^k}{k!}$$

$$= 1 - e^{-\lambda t} e^B$$

$$H(t) = 1 - e^{B-\lambda t}$$

Now the probability density function of T is obtained by

$$\frac{d}{dt}[H(t)] = \frac{d}{dt}\{1 - e^{B-\lambda t}\}$$

$$h(t) = -\frac{d}{dt}\{1 - e^{B-\lambda t}\}$$

$$= -\frac{d}{dt}\{1 - e^{B-\lambda t}\}$$

$$= -(A\lambda - \lambda)\, e^{t(A\lambda - \lambda)}$$

$$h(t) = (\lambda - A\lambda)\, e^{t(A\lambda - \lambda)}$$

Now, the mean time to cross the Antigenic diversity threshold is obtained by

$$E(T) = \int_0^\infty t(\lambda - A\lambda)e^{-t(\lambda - A\lambda)}dt$$

$$= (\lambda - A\lambda)\int_0^\infty t\, e^{-t(\lambda - A\lambda)}dt$$

$$= (\lambda - A\lambda)^* \frac{1}{(\lambda - A\lambda)^2}$$

$$i.e., E(T) = \frac{1}{(\lambda - A\lambda)}$$

Also,

$$E(T^2) = \int_0^\infty (t)^2 (\lambda - A\lambda)e^{-t(\lambda - A\lambda)}dt$$

$$= (\lambda - A\lambda)\int_0^\infty t^2\, e^{-t(\lambda - A\lambda)}dt$$

$$= (\lambda - A\lambda) * \frac{2}{(\lambda - A\lambda)^3}$$

$$E(T^2) = \frac{2}{(\lambda - A\lambda)^2}$$

The variance of the time to CADT is obtained by,

$$V(T) = E(T^2) - [E(T)]^2$$

$$= \frac{2}{(\lambda - A\lambda)^2} - \left(\frac{1}{(\lambda - A\lambda)}\right)^2$$

$$i.e., V(T) = \frac{1}{(\lambda - A\lambda)^2}$$

It may be interesting thing to notice that the distribution of time to cross the antigenic diversity threshold follows exponential distribution with parameter λ.

The values mean and variance of the time to CADT based on the formulate derived above are reported to in Table 1 and Table 2, keeping 'a' fixed.

Table 1
Mean time to CADT
(a = 1)

Fig. - 1

λ	$\beta = 0.3$	$\beta = 0.5$	$\beta = 0.7$	$\beta = 0.9$
1	19.397	9.139	5.921	4.541
2	9.435	4.487	2.897	2.324
3	6.324	3.534	1.987	1.564
4	4.765	2.324	1.498	1.243
5	3.865	1.756	1.234	0.913
6	3.335	1.653	0.996	0.842
7	2.986	1.642	0.853	0.746
8	2.321	1.112	0.737	0.654
9	2.1884	1.111	0.645	0.532
10	1.989	0.9021	0.597	0.4486

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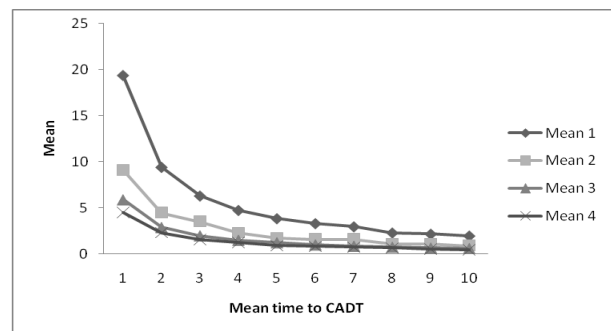
Table 2
Variance time to CADT
(a = 1)

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Fig.- 2

λ	$\beta = 0.3$	$\beta = 0.5$	$\beta = 0.7$	$\beta = 0.9$
1	367.2429	81.4562	36.7655	19.8786
2	89.3857	20.4541	8.4331	4.9765
3	39.8986	9.2309	3.8654	2.2123
4	22.4655	5.9875	2.1233	1.2532
5	14.3761	3.4307	1.3876	0.8164
6	9.9546	2.5646	0.9432	0.5641
7	7.3654	1.7861	0.7123	0.4324
8	5.5988	1.2546	0.5231	0.3143
9	4.4307	1.1231	0.4114	0.249
10	3.5098	0.8543	0.3542	0.189
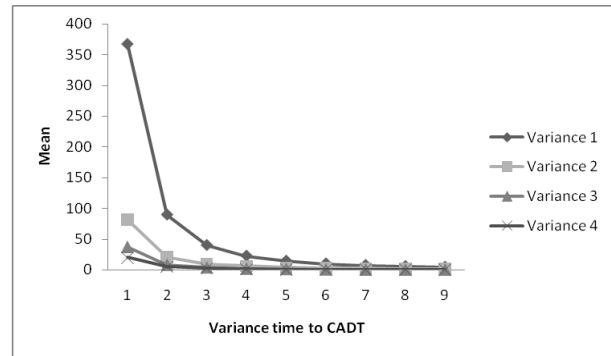
MODEL 2:

The random variable Y which denotes the antigenic diversity threshold has the p. d. f.

$$h_1(y) = \theta_1 e^{-\theta_1 y} \quad if \leq y_0$$
$$h_2(y) = \theta_2 e^{-\theta_2 y} \; e^{y_0(\theta_2 - \theta_1)} \quad if > y_0$$

Where y_0 is the truncation point for Y

Now the probability in 'K' contacts in (0.t] the antigenic diversity does not cross the threshold is given by

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

$$= \int_0^\infty g_k(x) \left[\overline{H_1(x)} + \overline{H_2(x)}\right] dx \tag{1}$$

Case (i) $y \leq y_0$

$$H_1(y) = \int_0^y \theta_1 e^{-\theta_1 u} \; du$$

$$= 1 - e^{-\theta_1 y}$$

$$\therefore \overline{H_1(x)} = e^{-\theta_1 x}$$

Case (ii) $y > y_0$

Now $H_2(y) = \int_0^y h(u) \; du$

$$= \int_0^{y_0} \theta_1 e^{-\theta_1 x} \; dx + \int_{y_0}^y \theta_2 e^{-\theta_2 x} \; e^{y_0(\theta_2 - \theta_1)} \; dx$$

$$H_2(y) = 1 - e^{-\theta_2 y} \; e^{y_0(\theta_2 - \theta_1)}$$

and so, $\overline{H_2}(y) = e^{y_0(\theta_2 - \theta_1)} e^{-\theta_2 y}$

$$\therefore \overline{H_1}(x) + \overline{H_2(x)} = e^{-\theta_1 x} + e^{y_0(\theta_2 - \theta_1)} e^{-\theta_2 x} \tag{2}$$

The survivor function is given by

S (t) = P [T > t] = Pr [that there are exactly 'K' contacts (0, t] and the total antigenic   diversity does cross the threshold]

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \; P\left[\sum_{i=1}^{K} X_i < Y \right]$$

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \; . \int_0^{\infty} g_k(x) \left[\overline{H_1(x)} + \overline{H_2(x)} \right] dx$$

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \; \left\{ \int_0^{\infty} g_k(x) \, e^{-\theta_1(x)} \, dx + \int_0^{\infty} e^{y_0(\theta_2-\theta_1)} . e^{-\theta_2 x} \, dx \right\}$$

$$= \left[1 - [1 - g^*(\theta_1)] \sum_{k=0}^{\infty} F_k(t) \, g^*(\theta_1)^{k-1} \right]$$

S(t) $$ + e^{y_0(\theta_2-\theta_1)} \left[1 - [1 - g^*(\theta_2)] \sum_{k=1}^{\infty} F_k(t) \, g^*(\theta_2)^{k-1} \right] $$ (3)

On Simplification

Now   L(t) $= 1 - S(t)$

$$= [1 - g^*(\theta_1)] \sum_{k=1}^{\infty} F_k(t) \, g^*(\theta_1)^{k-1} + e^{y_0(\theta_2-\theta_1)} [1 - g^*(\theta_2)] \sum_{k=1}^{\infty} F_k(t) \, g^*(\theta_2)^{k-1}$$

Taking Laplace Transform

$$L^*(s) = \left\{ [1 - g^*(\theta_1)] \sum_{k=1}^{\infty} f^*(s)^k \; [g^*(\theta_1)]^{k-1} \right.$$

$$\left. + e^{y_0(\theta_2-\theta_1)} [1 - g^*(\theta_2)] \sum_{k=1}^{\infty} f^*(s)^k [g^*(\theta_2)]^{k-1} \right\}$$

and we have

$$l^*(s) = \frac{[1 - g^*(\theta_1)] f^*(s)}{[1 - g^*(\theta_2) f^*(s)]} + e^{y_0(\theta_2-\theta_1)} \frac{[1 - g^*(\theta_1)] f^*(s)}{[1 - g^*(\theta_2) f^*(s)]}$$ (4)

On simplification

Let us assume that $g(.) \sim \exp(\lambda)$

$$\therefore \; g^*(\theta_1) = \frac{\lambda}{\lambda + \theta_1} \quad g^*(\theta_2) = \frac{\lambda}{\lambda + \theta_2}$$

Let $f(.) \sim \exp(\mu)$

$$\therefore \; f^*(s) = \frac{\mu}{\mu + s}$$

Substituting the values in (4)

$$l^*(s) = \frac{\left[1 - \frac{\lambda}{\lambda + \theta_1} \frac{\mu}{\mu + s} \right]}{\left[1 - \frac{\lambda}{\lambda + \theta_2} \frac{\mu}{\mu + s} \right]} - e^{y_0(\theta_2-\theta_1)} + e^{y_0(\theta_2-\theta_1)} \frac{\left[1 - \frac{\lambda}{\lambda + \theta_1} \frac{\mu}{\mu + s} \right]}{\left[1 - \frac{\lambda}{\lambda + \theta_2} \frac{\mu}{\mu + s} \right]}$$

$$= \frac{-(\theta_1\mu)}{(\lambda + \theta_1)(\mu + s) - \lambda\mu} - e^{y_0(\theta_2-\theta_1)} \frac{(\theta_2\mu)}{(\lambda + \theta_2)(\mu + s) - \lambda\mu}$$

$$= \frac{-(\theta_1 \mu) e^{y_0(\theta_2 - \theta_1)}}{\lambda s + \theta_1 \mu + \theta_1 s} + e^{y_0(\theta_2 - \theta_1)} \frac{(\theta_2 \mu)}{\lambda s - \theta_2 \mu + \theta_2 s}$$

(5)

$$E(T) = -\frac{dl(s)}{ds}$$

Put $s = 0$

$$E(T) = \frac{e^{y_0(\theta_2 - \theta_1)}(\lambda + \theta_2)}{(\theta_2 \mu)} - \frac{e^{y_0(\theta_2 - \theta_1)}(\lambda + \theta_1)}{(\theta_1 \mu)}$$

(6)

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

$$= \frac{-2(\lambda + \theta_1)^2 \; e^{y_0(\theta_2 - \theta_1)}}{(\theta_2 \mu)^3} + \frac{-2(\lambda + \theta_2)^2 \; e^{y_0(\theta_2 - \theta_1)}}{(\theta_1 \mu)^2}$$

(7)

$$E(T^2) = \left[\frac{2(\lambda + \theta_2)^2 \; e^{y_0(\theta_2 - \theta_1)}}{(\theta_2 \mu)^2} - \frac{-2(\lambda + \theta_1)^2 \; e^{y_0(\theta_2 - \theta_1)}}{(\theta_1 \mu)^2} \right]$$

(8)

Hence, $\quad V(T) - E(T^2) - [E(T)]^2$

$$V(T) = \frac{2e^{y_0(\theta_2 - \theta_1)}}{\mu^2} \left[\left(\frac{\lambda + \theta_2}{\theta_2} \right)^2 \quad \left(\frac{\lambda + \theta_2}{\theta_-} \right)^2 \right] \quad \frac{e^{2y_0(\theta_2 - \theta_1)}}{\mu^2} \left[\left(\frac{\lambda + \theta_1}{\theta_-} \right) \quad \left(\frac{\lambda + \theta_2}{\theta_2} \right) \right]^2$$

(9)

On Simplification

Table- 3

μ=1.0, y₀=15, θ₁= 1.2, θ₂= 0.2		
λ	E(T)	V(T)
2	2.60E-06	6.97E-05
4	5.15E-06	2.58E-04
6	7.70E-06	5.66E-04
8	1.02E-05	9.92E-04
10	1.28E-05	1.54E-03
12	1.53E-05	2.20E-03
14	1.79E-05	2.99E-03
16	2.04E-05	3.89E-03
18	2.29E-05	4.91E-03
20	2.55E-05	6.05E-03

Fig.- 3
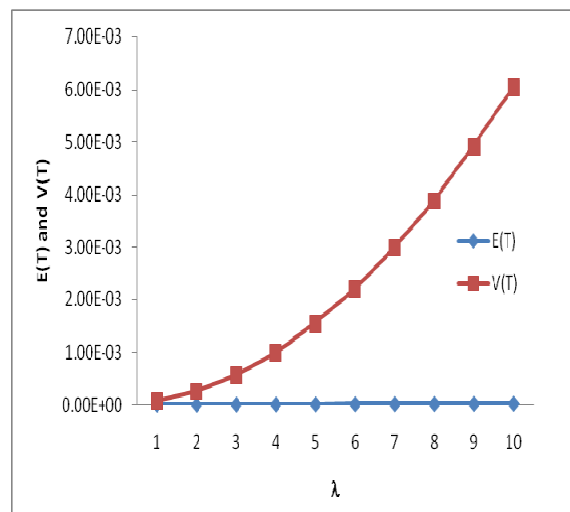
Table- 4

μ	E(T)	V(T)
$\lambda=1.0$, $y_0 =15$, $\theta_1= 1.2$, $\theta_2= 0.2$
1	1.33E-06	1.99E-05
2	6.63E-07	4.99E-06
3	4.42E-07	2.22E-06
4	3.31E-07	1.25E-06
5	2.65E-07	7.99E-07
6	2.21E-07	5.55E-07
7	1.89E-07	4.08E-07
8	1.66E-07	3.12E-07
9	1.47E-07	2.47E-07
10	1.33E-07	1.99E-07

Fig.-4
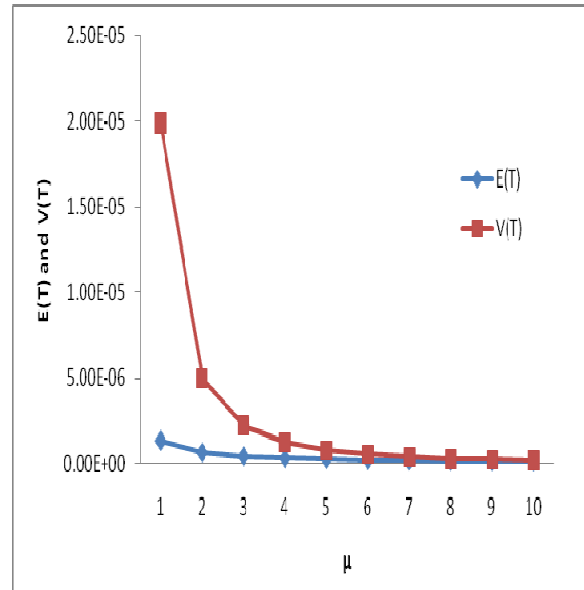
Table-5

	E(T)	V(T)
$\mu=1.0$, $y_0 =15$, $\lambda= 1.0$, $\theta_2= 0.2$
1.2	1.27E-06	1.99E-05
1.4	6.53E-08	1.01E-06
1.6	3.32E-09	5.06E-08
1.8	1.68E-10	2.54E-09
2	8.46E-12	1.27E-10
2.2	4.25E-13	6.34E-12
2.4	2.14E-14	3.17E-13
2.6	1.07E-15	1.58E-14
2.8	5.36E-17	7.89E-16
3	2.68E-18	3.94E-17
1.2	1.27E-06	1.99E-05

Fig.-5
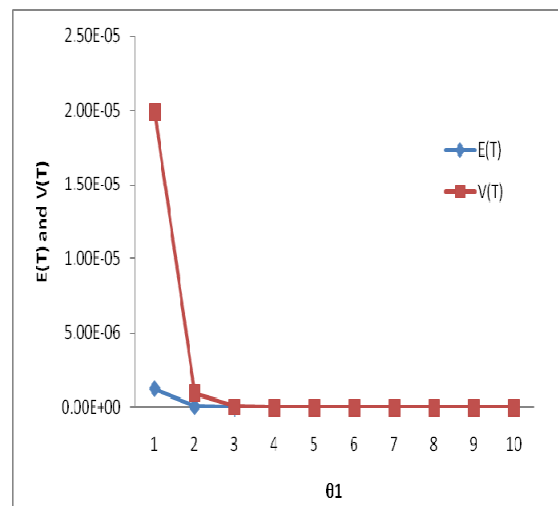
Table-6

	E(T)	V(T)
$\lambda=1.0$, $y_0 =15$, $\theta_1= 1.2$, $\mu = 1.0$
0.2	6.26E-07	1.61E-05
0.4	1.27E-06	1.99E-05
0.6	3.43E-06	4.23E-05
0.8	1.02E-05	1.09E-04
1	3.21E-05	3.11E-04
1.2	1.03E-04	9.26E-04
1.4	3.29E-04	2.81E-03
1.6	1.03E-03	8.43E-03
1.8	3.09E-03	2.43E-02
2	8.29E-03	6.36E-02
0.2	6.26E-07	1.61E-05

Fig.-6
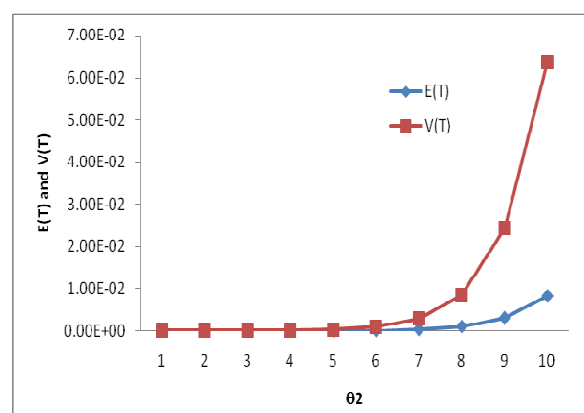
CONCLUSION:

From model 1, it could be seen from Fig. I that the expected time to CADT decreases sharply as the contact rate increases. This implies that decreasing the frequency of sexual contacts with an infected partner may lead to the elongation of time to CADT. In the case of variance it may be observed in Fig. 2 as the β value increases the corresponding variance decreases. Also as the contact rate increases, the variance becomes negligible. From model 2, as the value of λ which is the parameter of the exponential distribution of the random variable X denoting the contribution to antigenic diversity increases then E(T) increases very marginally. This is due to fact that as λ increases then $E(X) = 1/\lambda$ decreases since X follows exponential distribution. Hence the average amount of contribution to antigenic diversity in successive contacts is less and so it takes more time for seroconversion. This is indicated in Table 3 and Fig.3. As λ increases V (T) also increases. The random variable U_i denoting the interarrival times between contacts follows exponential distribution with parameter μ. As μ increases then $E (U) = 1/\mu$ decreases and this implies that in (0, t) the contacts will be more frequent. Hence then is greater contribution to antigenic diversity so E(T) decreases or indicated in Table 4 and Fig. 4.The variance V(T) also decreases. If θ_1 which is the parameter of the threshold distribution prior to the truncation point y_0, increases, then E(T) decreases. The decrease is very small and marginal. This is due to the fact that Y follows exponential distribution with θ_1 prior to y_0. Hence $E(Y) = 1/\theta_1$ decreases as θ_1 increases. Hence the threshold will be smaller. Hence it takes less of time to cross the threshold and therefore E(T) decreases V(T) also shows a marginal decrease. This is indicted in Table 5 and Fig. 5. The random variable Y follows exponential with parameter θ_2 after the truncation point y_0, and $E(Y) = 1/\theta_2$. Hence the threshold level decreases as θ_2 increases. So E(T) will be decreasing consequently. This is indicated in Table 6 and Fig. 6. V(T) also shows a increase.

DISCUSSION:

HIV infection and AIDS is a very serious problem shaking almost all the countries of the World. Remarkable amount of money has been spent by the nations to prevent the spread of HIV, for creating awareness among the people and to find effective medication or vaccine against AIDS. Making a scientific studies upon the various aspects of HIV infection. In such studies crossing the antigenic diversity threshold is an important event in the sense that it gives the most likely time for the development of AIDS condition in a infected person. Various characterization of the distribution derived can be studied as a further extension work of this thesis. Also the impact of the anti retro viral drugs to elongate the time to get AIDS can also be incorporated. Such studies would give ideal models for the practical applications and which in term would be highly useful for the society and mankind.

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