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RESEARCH ARTICLE

ESTIMATION OF EXPECTED TIME TO SEROCONVERSION DUE TO EITHER ANTIGENIC DIVERSITY OR VIRULENCE WHEN VIRULENCE DISTRIBUTION UNDERGOES A CHANGE

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ABSTRACT

The spread of HIV is a major issue which has received the attention of the medical personnel, mathematicians and also the people in the government. The rate of spread is really alarming. Till this day no medicine for complete cure is available. The mathematicians and statisticians use stochastic models to study the different aspects of this infection. An interesting aspect of study is to estimate the expected time to seroconversion using the concept of antigenic diversity. In this paper using two thresholds namely antigenic diversity and virulence thresholds expected time to seroconversion is found out under the assumption that the seroconversion occurs if any one of the two thresholds is crossed due to accumulation of antigens on successive occasions of exposure. The antigenic diversity threshold is taken to be a random variable which undergoes of change distribution. Numerical illustrations are also provided.

INTRODUCTION

The incidence and spread of Human Immune Deficiency Virus (HIV) and the consequent Acquired Immune Deficiency Syndrome (AIDS) is really a matter of great concern in many of the countries. The spread of HIV is at an alarming rate and the complete cure from the same is not yet available. The people in the field of medicine strive hard and do research to find a medicine to cure the disease. The use of mathematical namely stochastic models to describe the rate of spread of epidemic, to determine the likely time at which a person becomes seropositive and also the likely time at which a person becomes an AIDS case are all area of interest in medical research. In the present work the expected time to seroconversion is obtained using the stochastic model which is based on the shock model approach. In doing so, the two thresholds namely antigenic diversity threshold and virulence threshold are assumed. Antigenic diversity is the divergence of antigens so that the attack on the immune system is more pronounced. Virulence threshold expresses the intensity of virulence of the invading pathogens beyond which the human immune system fails. Several authors have studied the concept of virulence for example Levin and Svanborg Eden (1990), Weiss (2002) and Graham *et al.* (2005). Using the concept of antigenic diversity threshold and virulence threshold the expected time to seroconversion is derived. The shock model and cumulative damage process has been discussed by Esary *et al*. (1973).

Assumptions

1. A person is exposed to sexual contacts with an infected partner and on each occasion of contact the transmission of HIV takes place.
2. The mode of transmission of HIV on successive occasions results in the contribution to the antigenic diversity of the invading antigens. Also there is increase in the virulence of the invading antigens.
3. As and when the total antigenic diversity crosses a particular level called the antigenic diversity threshold, then the seroconversion takes place. Similarly if the total virulence of the invading antigens crosses the virulence threshold, then the seroconversion will occur.
4. The crossing of both antigenic diversity threshold and virulence threshold simultaneously is considered to be an impossible event.
5. The two thresholds are random variables and are mutually independent.

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Notations

X_i	:	a random variable denoting the contribution to antigenic diversity on the i^{th} contact i=1,2,3,….,k and with probability density function g(.) with cumulative distribution function G(.)
Y_i	:	the increase in the virulence due to the i^{th} contact, i=1,2,3,….,k with probability density function q (.) and cumulative distribution function Q(.)
Z_1	:	a random variable denoting antigenic threshold and has probability density function h(.) and cumulative distribution function H(.)
Z_2	:	a random variable denoting the virulence threshold with probability density function m(.) and cumulative distribution function M(.)
U_i	:	a random variable denoting the inter arrival times between contact i=1,2,3,….,k with probability density function of f (.) and cumulative distribution function F(.)
$l^*(s)$	:	Laplace transform of $l(t)$
T	:	time to seroconversion

RESULTS

When the virulence threshold undergoes change of distribution.
The survivor function $S(t)$ is given by

$S(t) = P[T > t] = P$[The antigenic diversity as well as the virulence due to k successive contacts do not cross the respective thresholds]

$$\begin{aligned} S(t) &= P\left[\sum_{i=1}^{k} X_i < Z_1 \cap \sum_{i=1}^{k} Y_i < Z_2\right] \\ &= P\left[\sum_{i=1}^{k} X_i < Z_1\right] P\left[\sum_{i=1}^{k} Y_i < Z_2\right] \\ &= P[\text{There are } f_k \text{ constant in (0, t) and the total antigenic diversity as well} \\ &\quad \text{as total virulence do not cross the respective thresholds}] \end{aligned}$$

$$S(t) = \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \left[\int_0^{\infty} g_k(x) \overline{H(x)} d_x\right] \left[\int_0^{\infty} q_k(y) \overline{M(y)} d_y\right] \quad \dots (1)$$

Now, the random variable Z_2 denoting the virulence threshold undergoes change of distribution.
$Z_1 \sim h(.)$ with cumulative distribution function $H(.)$.
Z_1 is the antigenic diversity threshold and Z_2 does not undergoes changes
$Z_2 \sim m(.)$ with cumulative distribution function $M(.)$.
Suresh Kumar (2006) has dealt with the concept of the change of distribution of a random variable at a change point.
Now it is assume that the virulence threshold Z_2 has a change of distribution after a particular point called the truncation point τ which is a constant. The random variable Z_1 is such that

$$\begin{aligned} &Z_1 \sim exp(\theta_1) \\ &\underline{H(x)} = 1 - e^{-\theta_1 x} \\ &\overline{H(x)} = e^{-\theta_1 x} \qquad \dots (2) \\ &Z_2 \sim E_2(\theta_2) \end{aligned}$$

$$h(y) = \theta_1 e^{-y(\theta_1+\lambda)} + \frac{\lambda {\theta_2}^2 y}{(\lambda + \theta_1 - \theta_2)} e^{-\theta_2 y} - \frac{\lambda {\theta_2}^2}{(\theta_1 - \theta_2 + \lambda)^2} e^{-\theta_2 y} + \frac{\lambda {\theta_2}^2}{(\lambda + \theta_1 - \theta_2)^2} e^{-(\lambda+\theta_1)y}$$

$$H(y) = \theta_1 \int_o^y e^{-x(\theta_1+\lambda)}\, dx + \frac{\lambda {\theta_2}^2}{(\lambda + \theta_1 - \theta_2)} \int_o^y x e^{-\theta_2 x}\, dx - \frac{\lambda {\theta_2}^2}{(\theta_1 - \theta_2 + \lambda)^2} \int_o^y e^{-\theta_2 x}\, dx$$

$$+ \frac{\lambda {\theta_2}^2}{(\lambda + \theta_1 - \theta_2)^2} \int_o^y e^{-x(\lambda+\theta_1)}\, dx$$

$$I_1 = \theta_1 \int_o^y e^{-x(\theta_1+\lambda)}\, dx$$

$$= \theta_1 \left[\frac{e^{-x(\theta_1+\lambda)}}{-(\theta_1+\lambda)}\right]_o^y$$

$$= \theta_1 \left[\frac{e^{-y(\theta_1+\lambda)}}{-(\theta_1+\lambda)} + \frac{e^0}{(\theta_1+\lambda)}\right]$$

$$= \frac{\theta_1}{\theta_1+\lambda}\left[1 - e^{-y(\theta_1+\lambda)}\right]$$

$$I_2 = \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1-\theta_2)} \int_o^y x e^{-\theta_2 x}\, dx$$

$$= \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1-\theta_2)} \left[-x\frac{e^{-\theta_2 x}}{\theta_2} - \frac{e^{-\theta_2 x}}{{\theta_2}^2}\right]_o^y$$

$$= \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1-\theta_2)} \left[-y\frac{e^{-\theta_2 y}}{\theta_2} - \frac{e^{-\theta_2 y}}{{\theta_2}^2}\right] + \left[\frac{1}{{\theta_2}^2}\right]$$

$$= \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1-\theta_2)} \left[\frac{1-e^{-\theta_2 y} - y\theta_2 e^{-\theta_2 y}}{{\theta_2}^2}\right]$$

$$= \frac{\lambda}{(\lambda+\theta_1-\theta_2)} \left[1-e^{-\theta_2 y} - y\theta_2 e^{-\theta_2 y}\right]$$

$$I_3 = \frac{-\lambda {\theta_2}^2}{\theta_2(\theta_1-\theta_2+\lambda)^2}\left[1-e^{-\theta_2 y}\right]$$

$$I_4 = \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1)(\theta_1-\theta_2+\lambda)^2}\left[1-e^{-(\lambda+\theta_1)y}\right]$$

$$\overline{M(y)} = \frac{\theta_1}{\theta_1+\lambda}\left[1-e^{-y(\theta_1+\lambda)}\right] + \frac{\lambda}{(\lambda+\theta_1-\theta_2)}\left[1-e^{-\theta_2 y} - y\theta_2 e^{-\theta_2 y}\right]$$

$$-\frac{\lambda {\theta_2}^2}{\theta_2(\theta_1-\theta_2+\lambda)^2}\left[1-e^{-\theta_2 y}\right] + \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1)(\theta_1-\theta_2+\lambda)^2}\left[1-e^{-(\lambda+\theta_1)y}\right] \quad \ldots (3)$$

Where $p_1 = \frac{\theta_1}{\theta_1+\lambda}$, $q_1 = \frac{\lambda}{(\lambda+\theta_1-\theta_2)}$, $p_2 = \frac{\lambda {\theta_2}^2}{\theta_2(\theta_1-\theta_2+\lambda)^2}$ and $q_2 = \frac{\lambda {\theta_2}^2}{(\lambda+\theta_1)(\theta_1-\theta_2+\lambda)^2}$

$$\overline{M(y)} = p_1\left[1-e^{-y(\theta_1+\lambda)}\right] + q_1\left[1-e^{-\theta_2 y} - y\theta_2 e^{-\theta_2 y}\right] - p_2\left[1-e^{-\theta_2 y}\right]$$

$$+q_2\left[1-e^{-(\lambda+\theta_1)y}\right]$$

Now,
$S(t) = Pr\{$that there are exactly k contacts in $(0,t)$and the antigenic diversity, virulence developed do not cross the respective threshold levels$\}$

$$S(t) = \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]$$

$$\times \left[\int_0^{\infty} g_k(x)\, \overline{H(x)}\, dx\right]\left[\int_0^{\infty} g_k(y)\, \overline{M(y)}\, dy\right]$$

$$= \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\left[\int_0^{\infty} g_k(x)\, e^{-\theta_1 x}\, dx\right]\left[\int_0^{\infty} q_k(y)\left[p_1\left[1-e^{-y(\theta_1+\lambda)}\right] + q_1\left[1-e^{-\theta_2 y} - y\theta_2 e^{-\theta_2 y}\right]\right.\right.$$

$$\left.\left. - p_2\left[1-e^{-\theta_2 y}\right] + q_2\left[1-e^{-(\lambda+\theta_1)y}\right]\right]\, dy\right]$$

$$\ldots (4)$$

where $F_k(t) - F_{k+1}(t)$ denotes the probability that there are exactly k contacts in $(0,t)$ as per renewal theory.
Hence it is seen that

$$= \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\left[[g^*(\theta_1)]^k + p_1[q^*(\theta_1+\lambda)]^k + q_1[q^*(\theta_2)]^k - q_1\theta_2\frac{d}{d\theta_2}[q^*(\theta_2)]^k - p_2[q^*(\theta_2)]^k + q_2[q^*(\lambda+\theta_1)]^k\right]$$

$$= \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][g^*(\theta_1)]^k + p_1 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)[q^*(\theta_1 + \lambda)]^k]$$

$$+q_1 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\theta_2)]^k - q_1\theta_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\frac{d}{d\theta_2}[q^*(\theta_2)]^k$$

$$-p_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\theta_2)]^k + q_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\,[q^*(\lambda + \theta_1)]^k$$

$$= T_1 + T_2 + T_3 - T_4 - T_5 + T_6 \qquad \dots (5)$$

Now,

$$T_1 = \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][g^*(\theta_1)]^k$$

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

$$T_2 = p_1 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\theta_1 + \lambda)]^k$$

$$= p_1[1 - q^*(\theta_1 + \lambda)] \sum_{k=1}^{\infty} F_k(t)[q^*(\theta_1 + \lambda)]^{k-1}$$

$$T_3 = q_1 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\theta_2)]^k$$

$$= q_1[1 - q^*(\theta_2)] \sum_{k=1}^{\infty} F_k(t)[q^*(\theta_2)]^{k-1}$$

$$T_4 = -q_1\theta_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]\frac{d}{d\theta_2}[q^*(\theta_2)]^k$$

$$= q_1\theta_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)]k[q^*(\theta_2)]^{k-1}\frac{d}{d\theta_2}q^*(\theta_2)$$

$$T_5 = -p_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\theta_2)]^k$$

$$= -p_2[1 - q^*(\theta_2)] \sum_{k=1}^{\infty} F_k(t)[q^*(\theta_2)]^{k-1}$$

And

$$T_6 = q_2 \sum_{k=0}^{\infty}[F_k(t) - F_{k+1}(t)][q^*(\lambda + \theta_1)]^k$$

$$= q_2[1 - q^*(\lambda + \theta_1)] \sum_{k=1}^{\infty} F_k(t)[q^*(\lambda + \theta_1)]^{k-1}$$

Now, since $L(t) = 1 - S(t)$ and taking the Laplace transform we get,

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

$$+p_1[1 - q^*(\theta_1 + \lambda)]f^*(s) \sum_{k=1}^{\infty} [f^*(s)q^*(\theta_1 + \lambda)]^{k-1}$$

$$+q_1[1 - q^*(\theta_2)]f^*(s) \sum_{k=1}^{\infty} [f^*(s)q^*(\theta_2)]^{k-1}$$

$$+q_1\theta_2 \frac{d}{d\theta_2} q^*(\theta_2) \left[\sum_{k=0}^{\infty} k[f_k{}^*(t)][q^*(\theta_2)]^{k-1} - \sum_{k=0}^{\infty} k[f_{k+1}{}^*(t)][q^*(\theta_2)]^{k-1}\right]$$

$$-p_2[1 - q^*(\theta_2)]f^*(s) \sum_{k=1}^{\infty} [f^*(s)q^*(\theta_2)]^{k-1}$$

$$+q_2[1 - q^*(\lambda + \theta_1)]f^*(s) \sum_{k=1}^{\infty} [f^*(s)q^*(\lambda + \theta_1)]^{k-1}$$

$= A + B + C + D - E + F$ (on simplification) ... (6)

Where

$$A = \frac{[1 - g^*(\theta_1)]f^*(s)}{[1 - f^*(s)g^*(\theta_1)]}$$

Similarly

$$B = \frac{p_1[1 - q^*(\theta_1 + \lambda)]f^*(s)}{[1 - f^*(s)q^*(\theta_1 + \lambda)]}$$

$$C = \frac{q_1[1 - q^*(\theta_2)]f^*(s)}{[1 - f^*(s)q^*(\theta_2)]}$$

$$D = \frac{q_1\theta_2[1 - f^*(s)][f^*(s)]\frac{d}{d\theta_2}q^*(\theta_2)}{[1 - f^*(s)q^*(\theta_2)]^2}$$

$$E = -\frac{p_2[1 - q^*(\theta_2)]f^*(s)}{[1 - f^*(s)q^*(\theta_2)]}$$

$$F = \frac{q_2[1 - g^*(\lambda + \theta_1)]f^*(s)}{[1 - f^*(s)g^*(\lambda + \theta_1)]}$$

(on simplification)

Now $E(T)$ = Expected time to seroconversion

$-\frac{d}{ds}L^*(s)$given$s = o$

$$= -\left[\frac{dA}{ds} + \frac{dB}{ds} + \frac{dC}{ds} + \frac{dD}{ds} - \frac{dE}{ds} + \frac{dF}{ds}\right]_{s=0}$$

Let us assume that
$f(.) \sim \exp(\beta)$, $g(.) \sim \exp(\gamma)$, $q(.) \sim \exp(\delta)$

$$\therefore f^*(s) = \frac{\beta}{\beta + s}, g^*(\theta_1) = \frac{\gamma}{\gamma + \theta_1}, \qquad q^*(\theta_1 + \lambda) = \frac{\gamma}{\gamma + \theta_1 + \lambda}$$

$$g^*(\theta_2) = \frac{\gamma}{\gamma + \theta_2}, \qquad q^*(\lambda + \theta_1) = \frac{\gamma}{\gamma + \lambda + \theta_1}$$

Now $-\left[\frac{dA}{ds}\right]_{s=0}$

Now, it is seen that

$$A = \frac{[1 - g^*(\theta_1)]f^*(s)}{[1 - f^*(s)g^*(\theta_1)]}$$

$$= \frac{\left[1 - \frac{\gamma}{\gamma + \theta_1}\right]\left(\frac{\beta}{\beta + s}\right)}{\left[1 - \left(\frac{\beta}{\beta + s}\right)\left(\frac{\gamma}{\gamma + \theta_1}\right)\right]} = \frac{\beta\theta_1(\beta + s)^{-1} \Big/ \gamma + \theta_1}{(\beta + s)(\gamma + \theta_1) - \beta\gamma \Big/ (\beta + s)(\gamma + \theta_1)}$$

$$= \frac{\beta\theta_1}{\beta\theta_1 + s(\gamma + \theta_1)} = \beta\theta_1[\beta\theta_1 + s(\gamma + \theta_1)]^{-1}$$

$$= [\beta\theta_1] - 1[\beta\theta_1 + s(\gamma + \theta_1)]^{-2}(\gamma + \theta_1)$$

$$-\left[\frac{dA}{ds}\right]_{s=0} = \frac{\gamma + \theta_1}{\beta\theta_1}$$

Similarly

$$-\left[\frac{dB}{ds}\right]_{s=0} = \frac{p_1[\gamma + \theta_1 + \lambda]}{\beta[\theta_1 + \lambda]}$$

$$-\left[\frac{dC}{ds}\right]_{s=0} = \frac{q_1[\gamma + \theta_2]}{\beta[\theta_2]}$$

$$-\left[\frac{dD}{ds}\right]_{s=0} = \frac{q_1\gamma}{\beta\theta_2}$$

$$-\left[\frac{dE}{ds}\right]_{s=0} = -\frac{p_2[\gamma + \theta_2]}{\beta[\theta_2]}$$

$$-\left[\frac{dF}{ds}\right]_{s=0} = \frac{q_2[\gamma + \lambda + \theta_1]}{\beta[\lambda + \theta_1]}$$

$$E(T) = \frac{\gamma + \theta_1}{\beta\theta_1} + \frac{p_1[\gamma + \theta_1 + \lambda]}{\beta[\theta_1 + \lambda]} + \frac{q_1[\gamma + \theta_2]}{\beta[\theta_2]} + \frac{q_1\gamma}{\beta\theta_2} - \frac{p_2[\gamma + \theta_2]}{\beta[\theta_2]} + \frac{q_2[\gamma + \lambda + \theta_1]}{\beta[\lambda + \theta_1]}$$

Where $p_1 = \frac{\theta_1}{\theta_1 + \lambda}$, $q_1 = \frac{\lambda}{(\lambda + \theta_1 - \theta_2)}$, $p_2 = \frac{\lambda{\theta_2}^2}{\theta_2(\theta_1 - \theta_2 + \lambda)^2}$ and $q_2 = \frac{\lambda{\theta_2}^2}{(\lambda + \theta_1)(\theta_1 - \theta_2 + \lambda)^2}$

$$E(T) = \frac{\gamma + \theta_1}{\beta\theta_1} + \frac{\theta_1}{\theta_1 + \lambda}\left[\frac{[\gamma + \theta_1 + \lambda]}{\beta[\theta_1 + \lambda]}\right] + \frac{\lambda}{(\lambda + \theta_1 - \theta_2)}\left[\frac{[\gamma + \theta_2]}{\beta[\theta_2]}\right] + \frac{\lambda}{(\lambda + \theta_1 - \theta_2)}\left[\frac{\gamma}{\beta\theta_2}\right] - \frac{\lambda{\theta_2}^2}{\theta_2(\theta_1 - \theta_2 + \lambda)^2}\left[\frac{[\gamma + \theta_2]}{\beta[\theta_2]}\right] + \frac{\lambda{\theta_2}^2}{(\lambda + \theta_1)(\theta_1 - \theta_2 + \lambda)^2}\left[\frac{[\gamma + \lambda + \theta_1]}{\beta[\lambda + \theta_1]}\right] \quad \ldots (7)$$

$$E(T^2) = \left[\frac{d^2}{ds} L^*(s)\right]_{s=0}$$

$$\frac{d^2 A}{dS^2} = [\beta\theta_1](-1)(-2)[\beta\theta_1 + s(\gamma+\theta_1)]^{-3}(\gamma+\theta_1)^2$$

$$= 2[\beta\theta_1][\beta\theta_1 + s(\gamma+\theta_1)]^{-3}(\gamma+\theta_1)^2$$

$$= \frac{2[\beta\theta_1](\gamma+\theta_1)^2}{[\beta\theta_1 + s(\gamma+\theta_1)]^2}$$

$$\frac{d^2 A}{dS^2} = \frac{2(\gamma+\theta_1)^2}{[\beta\theta_1]^2}$$

Similarly

$$\frac{d^2 B}{dS^2} = \frac{2p_1[\gamma+\theta_1+\lambda]^2}{\beta^2[\theta_1+\lambda]^2}$$

$$\frac{d^2 C}{dS^2} = \frac{2q_1[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2}$$

$$\frac{d^2 D}{dS^2} = \frac{4q_1\gamma(\gamma+\theta_2)}{\beta^2[\theta_2]^2}$$

$$\frac{d^2 E}{dS^2} = -\frac{2p_2[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2}$$

$$\frac{d^2 F}{dS^2} = \frac{2q_2[\gamma+\lambda+\theta_1]^2}{\beta^2[\lambda+\theta_1]^2}$$

$$E(T^2) = \frac{2(\gamma+\theta_1)^2}{[\beta\theta_1]^2} + \frac{2p_1[\gamma+\theta_1+\lambda]^2}{\beta^2[\theta_1+\lambda]^2} + \frac{2q_1[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2} + \frac{4q_1\gamma(\gamma+\theta_2)}{\beta^2[\theta_2]^2} - \frac{2p_2[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2} + \frac{2q_2[\gamma+\lambda+\theta_1]^2}{\beta^2[\lambda+\theta_1]^2} \quad \dots (8)$$

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

$$V(T) = \left[\frac{2(\gamma+\theta_1)^2}{[\beta\theta_1]^2} + 2\left[\frac{\theta_1}{\theta_1+\lambda}\right]\frac{[\gamma+\theta_1+\lambda]^2}{\beta^2[\theta_1+\lambda]^2} + 2\left[\frac{\lambda}{(\lambda+\theta_1-\theta_2)}\right]\frac{[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2} + \left[\frac{\lambda}{(\lambda+\theta_1-\theta_2)}\right]\frac{4\gamma(\gamma+\theta_2)}{\beta^2[\theta_2]^2} - 2\left[\frac{\lambda{\theta_2}^2}{\theta_2(\theta_1-\theta_2+\lambda)^2}\right]\frac{[\gamma+\theta_2]^2}{\beta^2[\theta_2]^2} + 2\left[\frac{\lambda{\theta_2}^2}{(\lambda+\theta_1)(\theta_1-\theta_2+\lambda)^2}\right]\frac{[\gamma+\lambda+\theta_1]^2}{\beta^2[\lambda+\theta_1]^2}\right]$$

$$-\left[\frac{\gamma+\theta_1}{\beta\theta_1} + \frac{\theta_1}{\theta_1+\lambda}\left[\frac{[\gamma+\theta_1+\lambda]}{\beta[\theta_1+\lambda]}\right] + \frac{\lambda}{(\lambda+\theta_1-\theta_2)}\left[\frac{[\gamma+\theta_2]}{\beta[\theta_2]}\right] + \frac{\lambda}{(\lambda+\theta_1-\theta_2)}\left[\frac{\gamma}{\beta\theta_2}\right] - \frac{\lambda{\theta_2}^2}{\theta_2(\theta_1-\theta_2+\lambda)^2}\left[\frac{[\gamma+\theta_2]}{\beta[\theta_2]}\right] + \frac{\lambda{\theta_2}^2}{(\lambda+\theta_1)(\theta_1-\theta_2+\lambda)^2}\left[\frac{[\gamma+\lambda+\theta_1]}{\beta[\lambda+\theta_1]}\right]\right]^2 \quad \dots (9)$$

Numerical Examples

The following numerical example provides an idea of $E(T)$ and $V(T)$ due to changes in the values of different parameters.

Table 1 Variation in E (T) and V (T) for Changes in $\theta_1 \theta_2 = 0.5, \lambda = 0.8, \gamma = 1.0, \beta = 2.0$

θ_1	E(T)	V(T)
0.5	3.615	0.094
1.0	2.666	1.037
1.5	2.246	1.152
2.0	2.000	1.197
2.5	1.836	1.267

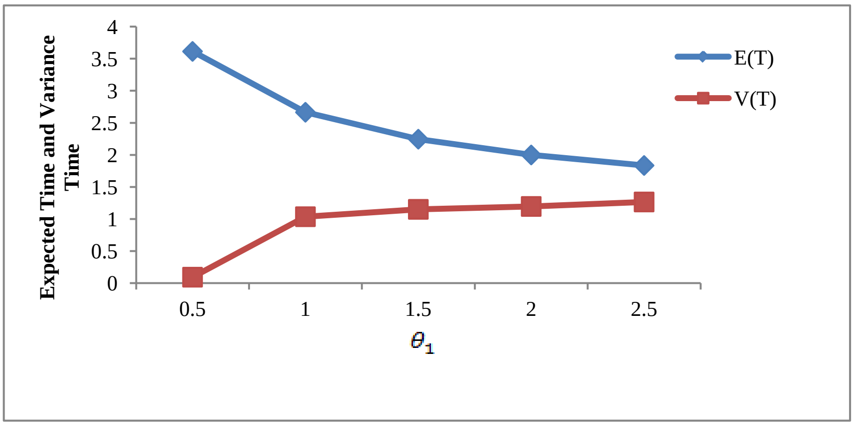

Figure 1 Variation in E (T) and V (T) for Changes in θ_1

Table 2 Variation in E (T) and V (T) for Changes in θ_2 $\theta_1 = 1.2, \lambda = 0.8, \gamma = 1.0, \beta = 2.0$

θ_2	E(T)	V(T)
0.5	2.246	1.152
1.0	1.898	1.092
1.5	1.786	0.921
2.0	1.723	0.756
2.5	1.681	0.563

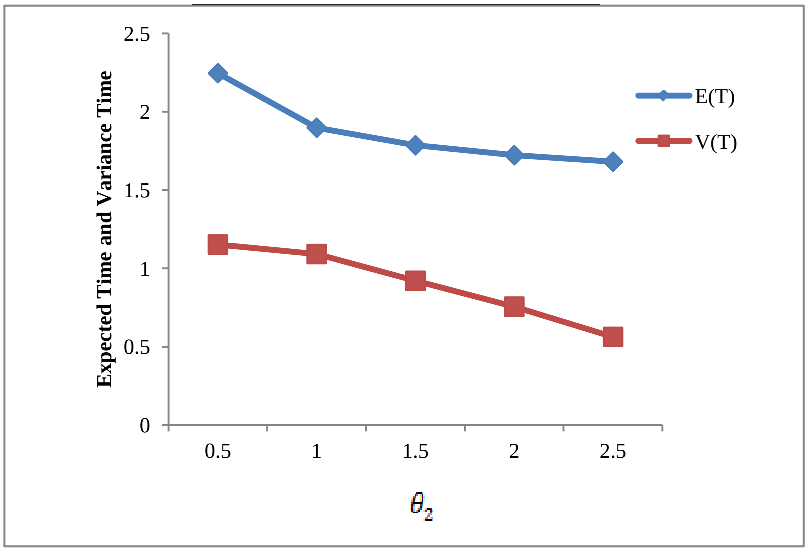

Figure 2 Variation in E (T) and V (T) for Changes in θ_2

Table 3 Variation in E (T) and V (T) for Changes in λ $\theta_1 = 1.2, \theta_2 = 0.5, \gamma = 1.0, \beta = 2.0$

λ	E(T)	V(T)
0.5	2.299	0.943
1.0	2.553	1.179
1.5	2.712	1.212
2.0	2.822	1.328
2.5	2.903	1.372

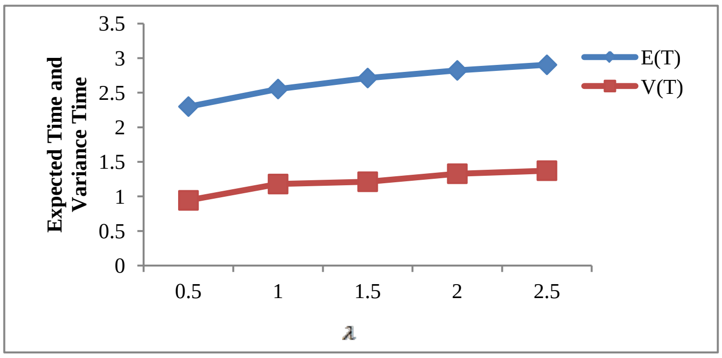

Figure3 Variation in E (T) and V (T) for Changes in λ

Table 4 Variation in E (T) and V (T) for Changes in β $\theta_1 = 1.2, \theta_2 = 0.5, \lambda = 0.8, \gamma = 1.0$

β	E(T)	V(T)
0.5	9.866	17.937
1.0	4.933	4.484
1.5	3.298	1.993
2.0	2.466	1.121
2.5	1.973	0.717

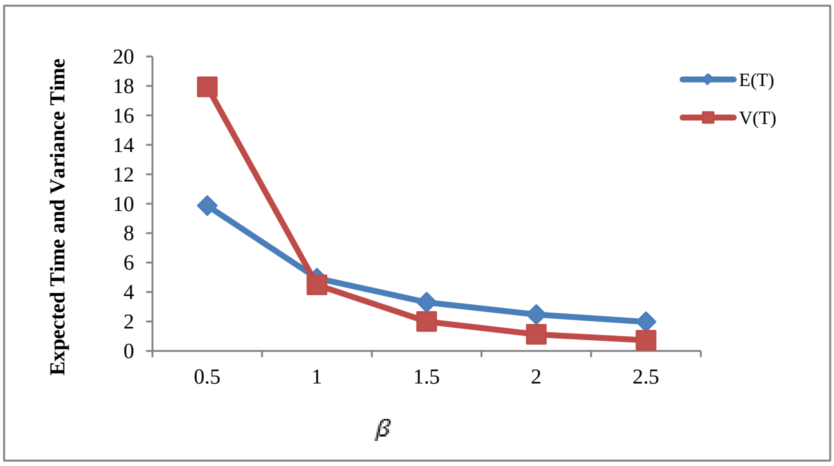

Figure 4 Variation in E (T) and V (T) for Changes in β

Table 5 Variation in E (T) and V (T) for Changes in γ $\theta_1 = 1.2, \theta_2 = 0.5, \lambda = 0.8, \beta = 2.0$

γ	E(T)	V(T)
0.5	1.733	0.280
1.0	2.466	1.121
1.5	3.200	2.522
2.0	3.933	4.484
2.5	4.666	7.006

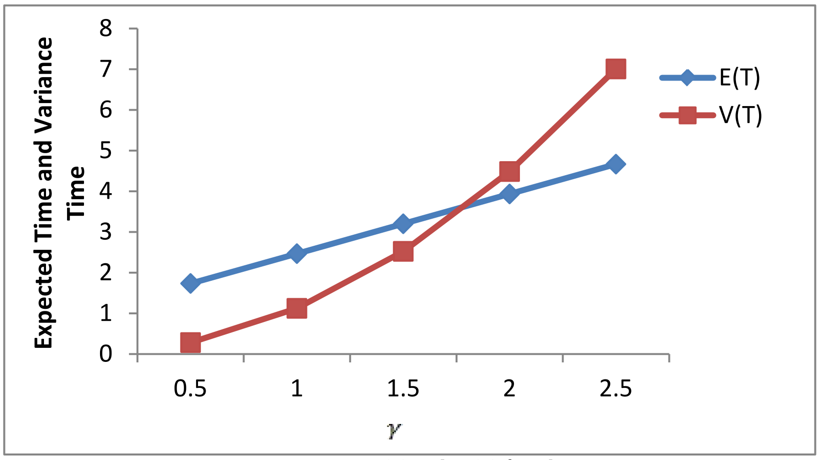

Figure 5: Variation in E (T) and V (T) for Changes in γ

CONCLUSION

On the basis of the numerical examples worked out for this model the following conclusions can be drawn.

1. It is assumed that the random variable Z_1 which represents the antigenic diversity threshold is assumed to follow exponential distribution which parameter θ_1. If θ_1 an increase with all the other parameters kept as fixed it is seen that E (T) decreases. This is due to fact that $E(Z_1) = \frac{1}{\theta_1}$ and so the threshold becomes as smaller as θ_1 increases. Therefore E (T) decreases. It is seen in table 1 and figure 1.
2. It is assumed that the random variable Z_2 which represents the virulence threshold is assumed to follow exponential distribution which parameter θ_2. So $E(Z_2) = \frac{1}{\theta_2}$ and so θ_2 increases the threshold becomes as smaller and so it takes less of time to cross the threshold. Hence E (T) decreases are seen in table 2 and figure 2.
3. The distribution of the random variable Z_1 denoting the antigenic diversity threshold undergoes the change of distribution after a truncation point τ which is itself is a random variable that follows the exponential with parameter λ so $(\tau) = 1/_{\lambda}$. As λ increases $E(\tau) = 1/_{\lambda}$ decreases. So E (T) increases as λ increases which are seen in table 3 and table 3.
4. It is assumed that the interarrival times between successive contacts is a random variable U_i which has the pdf as $f(.)$. It is assumed that $f(.)$ follows exponential with parameter β so that $(u) = 1/_{\beta}$. As β increases $E(u)$ becomes smaller. So that the number of contact will be more. So as β increases E (T) decreases and it is observed will table 4 and figure 4.
5. If the value of γ which is the parameter of the distribution of the random variable x_i denoting the contribution of antigenic diversity in the i^{th} contact shows an increase then $E(T)$ increases as observed in table 5 and figure 5. $V(T)$ also increases.

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