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Stability Analysis and Modelling of TB- HIV/AIDS co-infection with population dependent natural death rate

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Abstract

A differential equation model for TB-HIV/AIDS co-infection with population dependent natural death rate in finite population is analysed. Different conditions area derived for endemic and disease free equilibria. The basic reproduction numbers R_1 and R_2 for TB and HIV respectively exist then infection can persist if and only if $R_1>1$, and $R_2>1$. The population is disease free if $R_1<1$ and $R_2<1$. An equilibrium analysis of the model and local stability analysis for small perturbation about equilibrium values are discussed. The infection rate on spread of co-infection is evaluated numerically.

Keyword: transmission dynamics, co-infection, equilibrium analysis, stability analysis, numerical analysis

1. Introduction

The death toll in India from TB is still very significant and the number of HIV infected people is quite high in India. The HIV, human immunodeficiency virus, leads to acquired immunodeficiency syndrome (AIDS). According to global report at Geneva (2004), 40 million people, worldwide, are infected with HIV, and due to this disease about 20 million people have died in last two decades. About 14000 people are newly infected each day. The disease HIV is noncurable, and only with the help of the antiretroviral therapy (ART) life span of an infected person can be increased and can remain healthy before acquired full-blown AIDS. The risk of being HIV infected can be reduced by using less risky behavior like using safety measures in sexual activities or avoiding sharing of needle for injection drug users. A good number of adults have adopted safer sexual behavior in response to the AIDS epidemic (cf. Ahituv *et al.* 1996; Feinleib and Michael 1998). Mathematical models are playing a vital role in analyzing the spread of infectious diseases among the people (cf. Hethcote 2000; Singer 1996) and predicting the timing and extent of infection (cf. Mothashemi and Levins, 2001). Co-infection of TB and HIV are playing leading role in deaths from infectious diseases (cf. Corbett, 2003) [1]. The spread of HIV infection plays vital role in increasing the TB infection due to break down of the immune system. A person infected with TB may have latent or active infection. If the infection is latent then this infection will not take off the form of active disease due to the strong immune system. It may happen that a person will remain infected with latent TB for years or forever. For infectiveness of HIV - related TB, DOTS strategy has been recommended by WHO to control the TB (WHO, 2001). There are other ways to control the TB cases like reducing HIV infection by some intervention programmes, providing understanding of spreading HIV, treating the patients by HAART etc. (Santoro-Lopez *et al.*, 2002). When the susceptible individuals who are not infected with TB, get infection first, they enter into latent infection class of TB. The latent TB becomes active TB or TB disease at the rate of 0.001 per year in case of HIV negative (Vynnycky, 1996; Vynnycky and Fine, 1997; Styblo, 1991) [9, 10] and in case of HIV positive latent TB progresses TB disease at the rate of 0.1 per year (Schulzer *et al.*, 1992; Williams *et al.*, 2005) [6, 12]. Persons who are re-infected with TB, only 4.9% cases of TB leads to active disease for HIV-negatives and 50% cases of Latent TB progresses to TB disease in case of HIV- positive infection (Currie *et al.*, 2005, Qui Feng, 2010, Li and Wang, 2009) [2]. The HIV cases in the population increase more rapidly in the presence of other diseases particularly mTB; to control the spread of HIV, the mTB must be treated effectively (Naresh and TRipathi, 2005; William and Dye, 2003, Singh and jain, 2013) [4, 11].

The organization of this paper is as follows. In the section 2, mathematical model of TB-HIB/AIDS co-infection is described by a set of non-linear differential equations. In section 3, equilibrium analysis has been discussed. The stability analysis has been done in section 4. In section 5, the numerical results are provided. In the last section 6, conclusion is drawn.

2. The Mathematical Model

The total finite population is divided into four classes as susceptible class of persons, treatable malaria infected population, TB infected population, HIV infected class of persons and class of people with AIDS. Let S (t), I_1 (t), I_2 (t), and A (t) be susceptible population, malaria infected population, mTB infected population, HIV infected population and population with AIDS at time t, respectively.

We assume that susceptible individuals enter into the population from outside the system with constant birth rate r and constant immigration rate Q. The susceptible individuals become TB infected at the rate of α_1 and HIV infected at the rate of α_2. The TB infected individuals get HIV infection following the contact with HIV infective at the rate of α_3. Let ε be the rate at which the HIV infected individuals' progress to AIDS and υ be the death rate due to AIDS. Also let f(N) is the population dependent natural death rate from each class. μ denotes the rate at which individual leave the mTB (Mycobacterium tuberculosis) infected class, due to temporary immunity and again become susceptible. There is a constant emigration rate m >0 of individuals to other countries except for the AIDS patients. The rate of transition diagram of infectious diseases is shown in fig. 1.

The transition flow of diseases among various classes is governed by the system of equations as given below

$$\frac{dS}{dt} = Q + r - \frac{\alpha_1 S I_1 + \alpha_2 S I_2}{N} - mS - f(N)S + \mu I_1 \tag{1}$$

$$\frac{dI_1}{dt} = \frac{\alpha_1 S I_1}{N} - \frac{\alpha_3}{N} I_1 I_2 - f(N) I_1 - \mu I_1 - m I_1 \tag{2}$$

$$\frac{dI_2}{dt} = \frac{\alpha_2 S I_2}{N} + \frac{\alpha_3}{N} I_1 I_2 - f(N) I_2 - \varepsilon I_2 - m I_2 \tag{3}$$

$$\frac{dA}{dt} = \varepsilon I_2 - f(N) A - \upsilon A \tag{4}$$

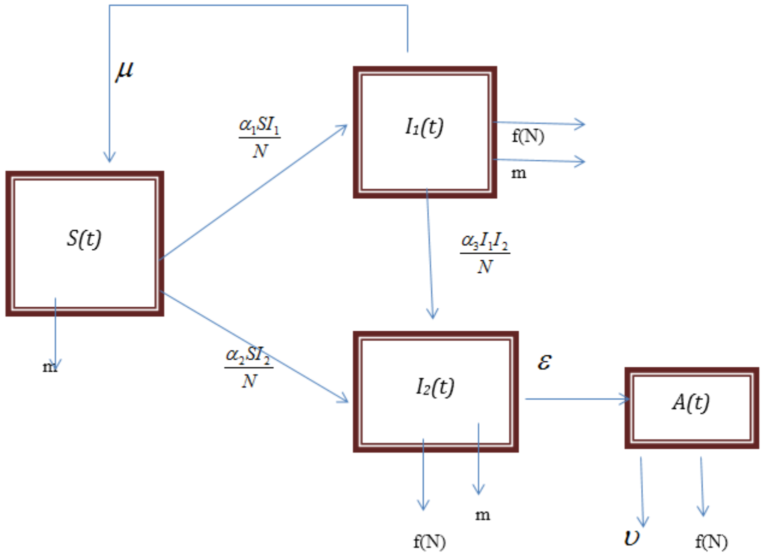

Fig 1: Graphical depiction of the transmission dynamics of the disease.

The total population at time t is denoted by $N(t) = S(t) + I_1(t) + +I_2(t) + A(t)$ and equations (1)-(4) can be written as

$$\frac{dN}{dt} = Q + r - \left(f(N) + m\right)N - \upsilon A \tag{5}$$

$$\frac{dI_1}{dt} = \frac{\alpha_1 (N - I_1 - I_2 - A)}{N} I_1 - \frac{\alpha_3}{N} I_1 I_2 - f(N) I_1 - \mu I_1 - m I_1 \tag{6}$$

$$\frac{dI_2}{dt} = \frac{\alpha_2 (N - I_1 - I_2 - A)}{N} I_2 + \frac{\alpha_3}{N} I_1 I_2 - f(N) I_2 - \varepsilon I_2 - m I_2 \tag{7}$$

$$\frac{dA}{dt} = \varepsilon I_2 - f(N) A - \upsilon A \tag{8}$$

3. Equilibrium Analysis

For equilibrium analysis, let us equate all the derivatives on the left hand side of equations (5)-(8) zero. We denote the equilibrium population of total population, mTB infected, HIV infected, and AIDS by S, I_1, I_2, A respectively. In view of this, we have

$$Q + r - \left(f(N) + m\right)N - \upsilon A = 0 \tag{9}$$

$$\frac{\alpha_1 (N - I_1 - I_2 - A)}{N} I_1 - \frac{\alpha_3}{N} I_1 I_2 - f(N) I_1 - \mu I_1 - m I_1 = 0 \tag{10}$$

$$\frac{\alpha_2(N-I_1-I_2-A)}{N}I_2+\frac{\alpha_3}{N}I_1I_2-f(N)I_2-\varepsilon I_2-mI_2=0 \qquad (11)$$

$$\varepsilon I_2-f(N)A-\upsilon A=0 \qquad (12)$$

We compute different equilibrium points as follows:

Theorem 1: There are four equilibrium values or points:

i) ***Equilibrium when population is free from the disease.***

The equilibrium point is obtain as

$$P_0\left(\frac{Q+r}{f(N)+m},0,0,\,0\right)$$

ii) ***When the population is mTB infected only.***

In this case $I_2=A=0$, as such equilibrium point is given by

$$P_1\left(\frac{Q+r}{f(N)+m},\frac{Q+r}{f(N)+m}\frac{1}{\alpha_1}\left(\alpha_1-(\mu+m+f(N))\right),0,0\right)$$

It is possible only when $\alpha_1>(\mu+m+f(N))$.

iii) ***When the population is HIV infected but free from mTB, then equilibrium point is obtained as***

$$P_2\left(\widehat{N},0,\widehat{I}_2,\widehat{A}\right)$$

where $\widehat{N}=\dfrac{1}{f(N)+m}\left(Q+r-\dfrac{\varepsilon\upsilon}{f(N)+m+\upsilon}\widehat{I}_2\right)$, $\widehat{A}=\dfrac{\varepsilon}{f(N)+m+\upsilon}\widehat{I}_2$

$$\widehat{I}_2=\frac{\dfrac{Q+r}{f(N)+m}\left(\alpha_2-(f(N)+m+\varepsilon)\right)}{\dfrac{m+f(n)+\upsilon+\varepsilon}{m+\upsilon+f(N)}\alpha_2+\dfrac{\varepsilon\upsilon}{(f(N)+m)(m+\upsilon+f(N))}\left(\alpha_2-(f(N)+m+\varepsilon)\right)}$$

This case exists only if $Q+r\succ\dfrac{\varepsilon\upsilon}{f(N)+m+\upsilon}\widehat{I}_2$ and $\alpha_2\succ(f(N)+m+\varepsilon$.

iv) ***When the population is co-infected of mTB-HIV,*** then the equilibrium point is

$$P^*\left(N^*,\,I_1^*,\,I_2^*,A^*\right)$$

where $N^*=\dfrac{1}{f(N)+m}\left(Q+r-\dfrac{\upsilon\varepsilon}{m+\upsilon+f(N)}I_2^*\right)$, $A^*=\dfrac{\varepsilon}{m+\upsilon+f(N)}I_2^*$,

$$I_1^*=\frac{\dfrac{Q+r}{f(N)+m}\left(\alpha_1-(\mu+m+f(N))\right)-\left(\dfrac{\upsilon\varepsilon}{(m+f(N))(f(N)+m+\upsilon)}\left(\alpha_1-(f(N)+m+\mu)\right)+\alpha_3+\dfrac{\upsilon+m+f(N)+\varepsilon}{\upsilon+m+f(N)}\alpha_1\right)I_2^*}{\alpha_1}$$

and

$$I_2^*=\frac{\dfrac{Q+r}{m+f(N)}\left[\left(\alpha_2-(f(N)+m+\varepsilon)\right)+\dfrac{\alpha_3-\alpha_2}{\alpha_1}\left(\alpha_1-(f(N)+m+\mu)\right)\right]}{\dfrac{f(N)+m+\upsilon+\varepsilon}{f(N)+m+\upsilon}\alpha_3+\dfrac{\upsilon\varepsilon}{(f(N)+m)(\upsilon+m+f(N))}\left[\left(\alpha_1-(f(N)+m+\mu)\right)+(\alpha_2-(\varepsilon+m+f(N)))+\alpha_3\dfrac{\alpha_3-\alpha_2}{\alpha_1}\right]}$$

In this case P* is positive only when $Q+r > \frac{\upsilon\varepsilon}{\upsilon+m+f(N)} I_2^*$, $\alpha_1 > (f(N)+m+\mu)$, $\alpha_2 > (f(N)+m+\varepsilon)$, and

$$\frac{Q+r}{f(N)+m}\left(\alpha_1-(\mu+m+f(N))\right) > \left(\frac{\upsilon\varepsilon}{(m+f(N))(f(N)+m+\upsilon)}\left(\alpha_1-(f(N)+m+\mu)\right)+\alpha_3+\frac{\upsilon+m+f(N)+\varepsilon}{\upsilon+m+f(N)}\alpha_1\right)I_2^*$$

4. Interpretation

First consider that it is always possible when the population has died e. i. $S=I_1=I_2=A=0$. The population maintains itself at a steady level when the disease has died out; the total number of susceptible individuals is $\frac{Q+r}{f(N)+m}$. From the equilibrium analysis, it is found that there are two basal reproduction numbers viz, $R_1 = \frac{\alpha_1}{f(N)+m+\mu}$ and $R_2 = \frac{\alpha_2}{f(N)+m+\varepsilon}$. If, $\alpha_1 > (f(N)+m+\mu)$ and $\alpha_2 > (f(N)+m+\varepsilon)$, then the infection of mTB and HIV respectively will die out and disease will not become endemic. Now we draw some other inferences from equilibrium values for co-infection of mTB-HIV. In this case also the population size is reduced from $\frac{Q+r}{f(N)+m}$ to $\frac{1}{f(N)+m}\left(Q+r-\frac{\upsilon\varepsilon}{m+\upsilon+f(N)}I_2^*\right)$. The higher contact rate α_1 (α_2) enhances the infection rate of mTB (HIV).

5. Stability Analysis

The stability analysis of equilibrium points by taking small perturbations is discussed as:

Case: I-II Equilibrium points when population is either free from infection or infected only by one disease.
For the case when population is free from disease, the equilibrium point P_0 is locally stable when $\alpha_1 > (f(N)+m+\mu)$ (i.e.$R_1<1$), and $\alpha_2 > (f(N)+m+\varepsilon)$ (i.e. $R_2 < 1$) otherwise unstable. But in case when population is infected by any single disease, the equilibrium points P_1 is unstable. R_1, and R_2 are the basal reproduction numbers for the malaria, and HIV infection respectively.

Case: III The equilibrium point P_2 is unstable but locally stable when $\alpha_1 > (f(N)+m+\mu)$ (i.e.$R_1<1$), $\alpha_2 > (f(N)+m+\varepsilon)$ (i.e.$R_2<1$), and provided $a_1a_2-a_3>0$ and $a_i(i=1,2,3)>0$.

Case: IV The points P* is locally stable, if it exists, Provided $b_i>0$, Routh-Hurwitch conditions are: $b_1 b_2 - b_3 > 0$ and $b_i(i=1,3,4)>0$ *and* $b_3(b_1b_2-b_3) > b_1^2 b_4$

6. Numerical Analysis

The numerical simulation and stability analysis of equations (1) to (5) have been given in this section. The equations are numerically solved with the help of Range-Kutta fourth order method by fixing different parameters in MATLAB software as follows. The natural death rate is considered as linear function as $f(N)=\lambda_1+\lambda_2 N$. The default parameter values are

$$Q=2000, r=2000,\ \alpha_1=0.925, \alpha_2=0.925, \alpha_3=0.285, \mu=0.030,\ m=0.0021$$

$$,\ \lambda_1=0.001, \lambda_2=0.000001, \varepsilon=0.2 \textit{ and } \upsilon=1.0$$

and the initial values are

N(0)=20000, $I_1(0)=3000$, $I_2(0)=4000$, $I_3(0)=4000$, A(0)=600

The numerical results are shown graphically in the figures 2-4.

In the fig.2, the distribution of population with time is shown for different classes with migration, birth rate and without recovery rates. It is seen that all sections population increases continuously and infected population increases initially because there is no migration and recovery. Therefore all infected ultimately develop AIDS and will ultimately meet the disease induced deaths. Thus the total population in this case will be eradicating after some time period.

In fig. 3 we see that the increment in ε the HIV infected population increases as they become the part of the full blown AIDS population. In fig. 4 the variation of AIDS population for different values ε. It is seen that with the increase in disease-induced death rate the AIDS population decreases.

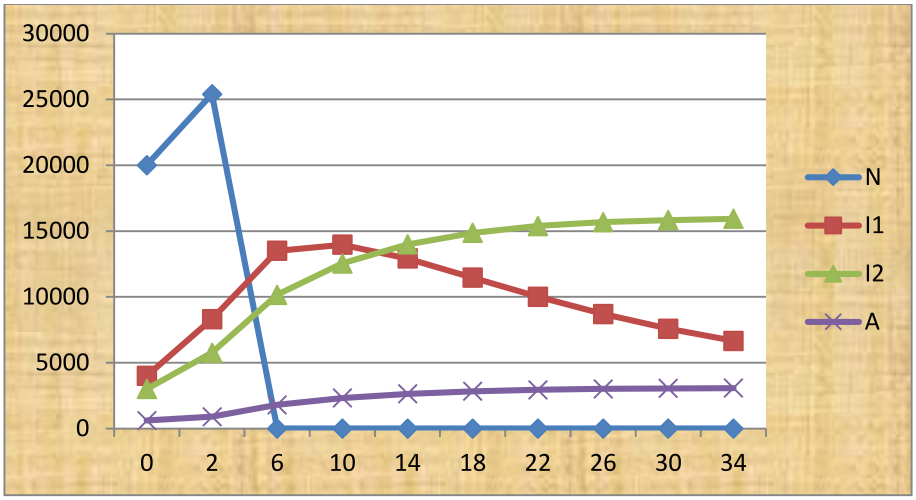

Fig 2: Variation of population in different classes (X-axis-population, Y-axis-time)

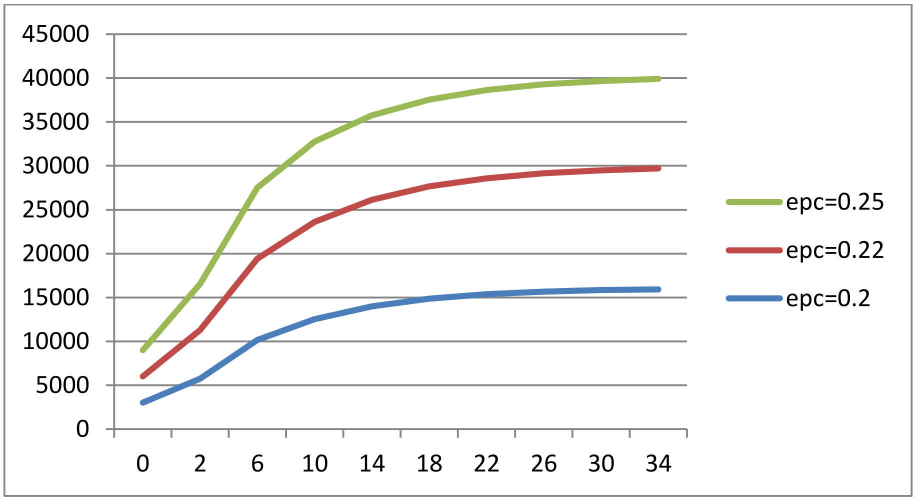

Fig 3: Variation of HIV infected population (X-axis-HIV infected population, Y-axis-time) for different values of ε rate HIV to AIDS.

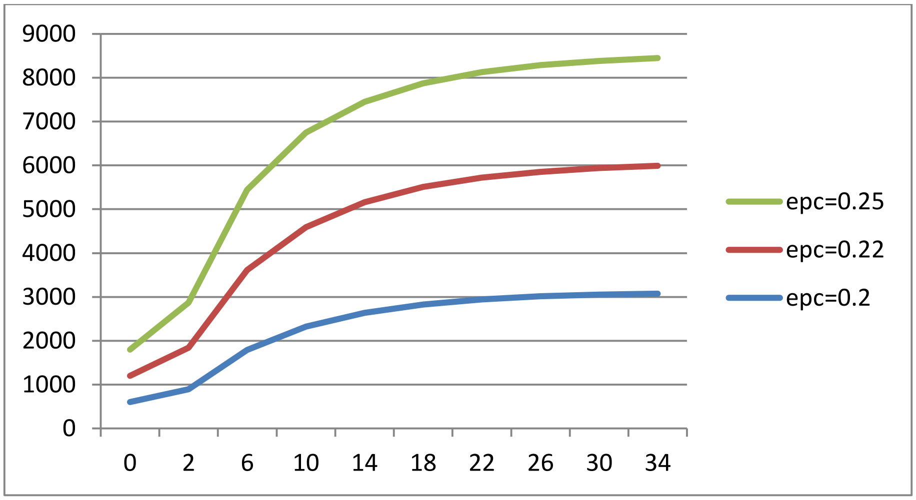

Fig 4: Variation of AIDS population (X-axis-AIDS population, Y-axis-time) for different values of ε rate HIV to AIDS.

7. Conclusion

The co-infection equilibrium point P^*(mTB-HIV) is always locally stable. Susceptible population enhances the infection rate. The disease becomes endemic due to immigration because immigration population is susceptible population. It is also found that higher temporary recovery rates increase the population of susceptible individuals. The infection may be control by reducing the susceptible population. Thus to reduce susceptible population, the permanent recovery is essential. The number of HIV infected cases increase due to the presence of other diseases like mTB. It is noticed that the HIV infection can be slowed down by treating mTB, effectively.

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