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AN APPROACH TO ESTIMATING THE TRANSMISSION COEFFICIENTS FOR AIDS AND FOR TUBERCULOSIS USING MATHEMATICAL MODELS

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A mathematical model is presented to simulate the interaction between Human Immunodeficiency Virus (HIV) and *Mycobacterium tuberculosis* (MTB) infections in a closed environment. The dynamics is formulated through a compartmental system of non-linear ordinary differential equations. The stability of the trivial equilibrium point or absence of infections and the endemic basins are analyzed based on the threshold values for the HIV and MTB transmission coefficients. In order to deal with the estimation of the transmission coefficients of HIV and MTB infections we consider the incarcerated individuals in the Female Penitentiary of São Paulo State, Brazil.

Keywords: AIDS; Tuberculosis; Interaction; Thresholds

1. INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a syndrome characterized by the interaction of the Human Immunodeficiency Virus (HIV) with other infections. HIV infection hinders immunity, favoring in this way a series of opportunist infections. One of them is tuberculosis (TB), which is caused by a bacillus of the type *Mycobacterium tuberculosis* (MTB).

The advent and further spreading of AIDS in a pandemic proportion had as a consequence the onset of TB in regions without any case reported in many years. Since then on TB is taken as an indicator of HIV infection. However, in developing countries, due to the endemic feature of TB, there is not a well established correlation between TB and AIDS. Particularly in Brazil, where TB still remains a serious public health problem,

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one cannot conclude that all individuals with TB are also HIV infected. Therefore, the study of the interaction of AIDS and TB diseases is of great importance for the understanding of this new TB outbreak and perhaps for finding strategies to curb it.

Many efforts have been made to explain the interaction between these diseases, particularly using mathematical models. Some are based on compartments and are being applied with great success in the study of the interaction between AIDS and TB [4,6,7,9–11]. In this study we present a mathematical model that describes the interaction between HIV and MTB infections in a closed environment, like a prison or mental institution. The dynamics of the model is formulated through a compartmental system described by non-linear ordinary differential equations, which represent the different subpopulations. Therefore, each compartment, in turn, represents one of the stages of the interaction between AIDS and TB [9].

This paper is divided as follows. In Section 2, we develop a model based on some biological features of the transmission between AIDS and TB diseases [6]. The trivial and non-trivial equilibrium points of the model are determined by using a control technique proposed here. Section 3 presents the stability analysis of the trivial equilibrium point and the endemic basins which are based on the threshold values for the HIV and MTB transmission coefficients. For instance, the trivial equilibrium point of the dynamical system provides thresholds under which both diseases, AIDS and TB, could be eradicated in a closed and controlled environment. Along the same line, conditions for eradication of a single disease and for both diseases to coalesce are obtained. In a confined environment, the previous mathematical model did not estimate the level of interaction between AIDS and TB among inmates. Clinical data, including follow up, is available for female inmates. Thus, in Section 4, we fit the model to these data, which were obtained from the incarcerated individuals in the Female Penitentiary of the State of São Paulo, Brazil [3]. As Ferreira *et al*. we also find that HIV can activate the MTB infection, and that TB worsens the clinical picture for HIV. In Section 5, we discuss epidemiological implications.

2. THE MODEL

The model is composed by seven compartments, each of them representing one of the stages of the interaction between AIDS and TB in a closed community. The working assumptions under which we have developed our model are as follows: (a) we are assuming ''mass-action principle'' [5]. The population is at every instant homogeneous; that is, there are no pockets of individuals sharing a certain pathology isolated from the rest and therefore, there is a homogeneous mixing; (b) the population is large enough in size to be modeled deterministically; (c) all transition rates of the model are non-negative and their values are initially estimated from the literature. The only ones which cannot be estimated from the literature are the per capita rates at which the individuals acquire infection, namely, the transmission coefficients for HIV and MTB infections; (d) MTB infection is transmitted by individuals with TB disease (pulmonary TB). Susceptible individuals become infected by contact with TB individuals. Once infected, these individuals either will develop TB (by direct progression or endogenous reactivation) or stay infected (non-infectious cases) for the rest of their life and we defined them as MTB infected or latent TB individuals; (e) HIV infection is transmitted by HIV-positive individuals. We assume that all forms of transmission of HIV (sexual

contact, intravenous drug use or vertical transmission) are clustered under a unique umbrella parameter given by the transmission coefficient for HIV infection. We will take it to be a constant independent of the total population; (f) susceptible individuals to HIV (healthy individuals, MTB infected individuals and TB individuals) after being infected with HIV infection will develop AIDS; (g) individuals with AIDS (with or without TB) are isolated and transferred to a Center for Infectious Diseases and AIDS to receive treatment. They are considered so ill that do not transmit the HIV infection, but the AIDS individuals with TB transmit MTB infection to AIDS individuals without TB; (h) the inflow of new susceptible individuals matches all of the outflow due to natural and differential deaths. Thus, the inflow and the outflow occur at equal rates; and (i) as mentioned before, our assumptions are based on general knowledge about closed environment like a prison or mental hospital. In developing countries, like Brazil, there is often overcrowding in these institutions. Owing to this, we assume that the total population has a constant size N and we will work with normalized unitary total population ($N=1$). The size of subpopulations (or state variables) in each compartment are fractions of this normalized population.

To clarify biological process we introduce for the state variables of the model the following notation: X_1, the healthy individuals susceptible to both HIV and MTB infections; X_2, the individuals who have been infected with MTB, but have no clinical illness and hence are non-infectious, that is, the MTB infected or latent TB individuals; Tb, individuals with TB disease; Y_1, the HIV-positive individuals without MTB infection; Y_2, the HIV-positive individuals with MTB infection; A, the individuals with AIDS but without TB and Atb, the individuals with AIDS and TB.

We also take the following parameters (dimension: year^{-1}) into account: ϕ is the input rate; β and λ are the transmission coefficients for HIV and MTB infections, respectively; ω is the incubation rates for AIDS without MTB infection; ξ is the incubation rate for AIDS with MTB infection; σ is the reactivation rate of TB disease; ρ is recovery rate of TB; μ is the natural mortality or remaining time in a closed community; α is the AIDS mortality rate and θ is the TB mortality rate.

These assumptions lead to following system of differential equations, which describes the dynamics of the transmission of both diseases:

$$\begin{cases} \dfrac{dX_1}{dt} = \phi - \beta X_1(Y_1 + Y_2) - \lambda X_1 Tb - \mu X_1 \\ \dfrac{dX_2}{dt} = \rho Tb + \lambda X_1 Tb - \beta X_2(Y_1 + Y_2) - (\sigma + \mu)X_2 \\ \dfrac{dTb}{dt} = \sigma X_2 - \beta Tb(Y_1 + Y_2) - (\rho + \mu + \theta)Tb \\ \dfrac{dY_1}{dt} = \beta X_1(Y_1 + Y_2) - \lambda Y_1 Tb - (\mu + \omega)Y_1 \\ \dfrac{dY_2}{dt} = \beta X_2(Y_1 + Y_2) + \lambda Y_1 Tb - (\xi + \mu)Y_2 \\ \dfrac{dA}{dt} = \omega Y_1 - \lambda A Atb - (\mu + \alpha)A \\ \dfrac{dAtb}{dt} = \xi Y_2 + \lambda A Atb + \beta Tb(Y_1 + Y_2) - (\mu + \alpha + \theta)Atb, \end{cases} \tag{1}$$

with $\phi = \mu + \theta(Tb + Atb) + \alpha(A + Atb)$, according to the constant population hypothesis. Therefore, summing up these equations, one gets $dN/dt = 0$, that is, the total population remains constant at all times. Because of the conservation law $X_1(t) + X_2(t) + Tb(t) + Y_1(t) + Y_2(t) + A(t) + Atb(t) = N(t) = 1$ for any $t \in R$, the first equation in (1) is decoupled from the last six, by using

$$X_1 = 1 - (X_2 + Tb + Y_1 + Y_2 + A + Atb) = 1 - \sum. \tag{2}$$

Hence, the system (1) can be rewritten as

$$\begin{cases} \dfrac{dX_2}{dt} = \rho Tb + \lambda\left(1 - \sum\right) Tb - \beta X_2(Y_1 + Y_2) - (\sigma + \mu)X_2 \\ \dfrac{dTb}{dt} = \sigma X_2 - \beta Tb(Y_1 + Y_2) - (\rho + \mu + \theta)Tb \\ \dfrac{dY_1}{dt} = \beta\left(1 - \sum\right)(Y_1 + Y_2) - \lambda Y_1 Tb - (\mu + \omega)Y_1 \\ \dfrac{dY_2}{dt} = \beta X_2(Y_1 + Y_2) + \lambda Y_1 Tb - (\xi + \mu)Y_2 \\ \dfrac{dA}{dt} = \omega Y_1 - \lambda A Atb - (\mu + \alpha)A \\ \dfrac{dAtb}{dt} = \xi Y_2 + \lambda A Atb + \beta Tb(Y_1 + Y_2) - (\mu + \alpha + \theta)Atb, \end{cases} \tag{3}$$

and the Eqs. (3) together with Eq. (2) will be referred to as MATB model. Note that (2) has been used to substitute for X_1 in the first equation of the system (1). Consequently, the analysis of system (3) and (1) leads to equivalent results when we consider the non-negative solutions that are of interest in this model.

To begin analysis of the MATB model we proceed as follows. We examine the disease-free steady state to determine the threshold parameters for which the diseases die out. By biological simplifications, we calculate the endemic equilibrium points and we here have several distinct threshold parameters for each of the diseases can persist. That is, we show the possibilities that one disease can remain endemic while the other is eradicated, the co-infection with AIDS and TB diseases, and the effects of opportunistic infections such as MTB on the course of HIV.

2.1. The Trivial Equilibrium Point

The important point we must analyze is whether there are threshold values for which the extinction of both AIDS and TB is warranted. This clearly means to study the stability of the trivial equilibrium point or disease-free steady state, namely P_ϕ, where one has $X_1 = N = 1$ and $X_2 = Tb = Y_1 = Y_2 = A = Atb = 0$. This is under the assumption that only healthy individuals are allowed to enter to the system.

The linearization matrix of the system (3) at the trivial equilibrium point is given by the following Jacobian matrix:

$$\mathbf{M}_{P_\phi} = \begin{bmatrix} -(\sigma+\mu) & \lambda+\rho & 0 & 0 & 0 & 0 \\ \sigma & -(\rho+\mu+\theta) & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta-(\mu+\omega) & \beta & 0 & 0 \\ 0 & 0 & 0 & -(\mu+\xi) & 0 & 0 \\ 0 & 0 & \omega & 0 & -(\mu+\alpha) & 0 \\ 0 & 0 & 0 & \xi & 0 & -(\mu+\alpha+\theta) \end{bmatrix}. \tag{4}$$

This matrix has six eigenvalues. Four of them are very easily computed as: $r_1 = -(\mu+\xi)$; $r_2 = -(\mu+\alpha)$; $r_3 = -(\mu+\alpha+\theta)$ and $r_4 = \beta-(\mu+\omega)$, while the other two (r_5 and r_6) are the eigenvalues of the submatrix:

$$\mathbf{B} = \begin{bmatrix} -(\sigma+\mu) & \lambda+\rho \\ \sigma & -(\rho+\mu+\theta) \end{bmatrix}, \tag{5}$$

whose *trace* $\mathbf{B} = -(\sigma+\mu+\rho+\mu+\theta)$ is always negative and $\det \mathbf{B}$ is positive when $\lambda < [\mu(\rho+\mu+\theta)+\sigma(\mu+\theta)]/\sigma$.

Now, given that all parameters of the model are assumed to be non-negative, the eigenvalues r_5 and r_6 have negative real part if $\lambda < [\mu(\rho+\mu+\theta)+\sigma(\mu+\theta)]/\sigma$, and the eigenvalue r_4 is negative if $\beta < \mu+\omega$. Thus, for the eigenvalues of the matrix (4) to have negative real part one needs:

$$\beta < \mu+\omega \equiv \beta_t \quad \text{and} \quad \lambda < \frac{\mu(\rho+\mu+\theta)+\sigma(\mu+\theta)}{\sigma} \equiv \lambda_t. \tag{6}$$

That is, the trivial equilibrium point P_ϕ is locally asymptotically stable only if both inequalities (6) are satisfied. From an epidemiological viewpoint this means that there are threshold values, β_t and λ_t, so that below these values both AIDS and TB tend toward extinction. If any of these two parameters exceeds its threshold value, then at least one disease will persist. We are now able to state this result in terms of the threshold parameters defined as:

$$R_0^{\mathrm{HIV}} = \frac{\beta}{(\mu+\omega)} = \frac{\beta}{\beta_t} \quad \text{and} \quad R_0^{\mathrm{TB}} = \frac{\sigma\lambda}{\mu(\rho+\mu+\theta)+\sigma(\mu+\theta)} = \frac{\lambda}{\lambda_t}. \tag{7}$$

The above result identifies the basic reproductive number for AIDS and TB, respectively. It shows that the diseases die out below the threshold values, that is, if $R_0^{\mathrm{HIV}} < 1$ and $R_0^{\mathrm{TB}} < 1$; whereas if $R_0^{\mathrm{HIV}} > 1$ and $R_0^{\mathrm{TB}} > 1$ both diseases could persist or remain endemic in the population. So we have showed the following result:

BIOTHEOREM 1 *The disease-free steady state P_ϕ is locally asymptotically stable if $R_0^{\mathrm{HIV}} < 1$ and $R_0^{\mathrm{TB}} < 1$.*

2.2. The Non-Trivial Equilibrium Points

If either parameters, β or λ, is over its threshold value, ($\beta > \beta_t$ or $\lambda > \lambda_t$, i.e., $R_0^{\mathrm{HIV}} > 1$ or $R_0^{\mathrm{TB}} > 1$), then the trivial equilibrium point is unstable. One should therefore

strongly suspect that there exist other equilibrium points besides the trivial equilibrium point. As a matter of fact, this is indeed the case. We will state, in terms of their biological interpretation, the different non-trivial equilibrium points or endemic states we are aware of. There might exist more of them.

Since we are dealing with the question of the ultimate prevalence of an endemic state of the diseases, it is more convenient we consider the proportion of individuals in the different classes rather than absolute number. For this, we assume that the prevalence (proportion of the total number cases) of disease decreases and vanishes after an effective disease control strategy is taken. Thus, we establish the following results:

BIOTHEOREM 2 *Assume that the prevalence of AIDS is remaining endemic while the prevalence of TB is vanishing in the community after control interventions for TB were taken. In mathematical terms this assumption means* $R_0^{\mathrm{HIV}} > 1$ *and* $Tb = 0$. *Then there are two endemic steady states biologically feasible given by* $P_1 = (X_1, 0, 0, Y_1, 0, A, 0)$ *and* $P_3 = (X_1, 0, 0, Y_1, 0, A, Atb)$.

Proof In our system of coupled non-linear differential equations denoted by MATB, let us take $Tb = 0$. The critical points of such a system are given by equations:

$$\begin{cases} -\beta X_2(Y_1 + Y_2) - (\sigma + \mu)X_2 = 0 \\ \sigma X_2 = 0 \\ \beta(Y_1 + Y_2)(1 - X_2 - Y_1 - Y_2 - A - Atb) - (\omega + \mu)Y_1 = 0 \\ \beta X_2(Y_1 + Y_2) - (\xi + \mu)Y_2 = 0 \\ \omega Y_1 - (\alpha + \mu)A - \lambda A Atb = 0 \\ \xi Y_2 + \lambda A Atb - (\mu + \alpha + \theta)Atb = 0. \end{cases}$$

From the above, one gets by direct inspection: $X_2 = 0$, $Y_2 = 0$ and either

$$\begin{cases} Atb = 0 & \text{(Case 1A)} \\ \text{or} \\ \lambda A - (\mu + \alpha + \theta) = 0 \Rightarrow A = \dfrac{(\mu + \alpha + \theta)}{\lambda} & \text{(Case 2A)} \end{cases}$$

Let us study each case in detail.

Case 1A If $Atb = 0$, then $Y_1 = ((\mu + \alpha)\ A)/\omega$. Now,

$$\begin{aligned} &\beta\, Y_1(1 - Y_1 - A) - (\mu + \omega)Y_1 = 0 \\ &\quad \Longleftrightarrow \beta\, Y_1 - \beta\, Y_1^2 - \beta\, Y_1 A - (\mu + \omega)Y_1 = 0, \end{aligned}$$

therefore, one either has $A = 0$ thus, $Y_1 = 0$ or

$$A = \frac{\omega[\beta - (\mu + \omega)]}{\beta(\mu + \alpha + \omega)}$$

thus,

$$Y_1 = \left[\frac{(\mu + \alpha)[\beta - (\mu + \omega)]}{\beta(\mu + \alpha + \omega)}\right].$$

Then, one has one non-trivial equilibrium point given by $P_1 = (X_1, 0, 0, Y_1, 0, A, 0)$, where

$$X_1 = \frac{1}{R_0^{\mathrm{HIV}}}$$

$$Y_1 = (\mu+\alpha)\left[\frac{\beta-(\mu+\omega)}{\beta(\mu+\alpha+\omega)}\right] = \frac{(\mu+\alpha)}{(\mu+\alpha+\omega)}\left[\frac{R_0^{\mathrm{HIV}}-1}{R_0^{\mathrm{HIV}}}\right] \tag{8}$$

$$A = \frac{\omega[\beta-(\mu+\omega)]}{\beta(\mu+\alpha+\omega)} = \frac{\omega}{(\mu+\alpha+\omega)}\left[\frac{R_0^{\mathrm{HIV}}-1}{R_0^{\mathrm{HIV}}}\right].$$

The biological feasibility of the critical point requires all state variable to be non-negative. Therefore, the point $P_1 = (X_1, 0, 0, Y_1, 0, A, 0)$ is biologically feasible, since for $R_0^{\mathrm{HIV}} > 1$, (β is assumed from the onset to be over threshold), one has X_1, Y_1 and A positives.

Case 1B If $A = (\mu+\alpha+\theta)/\lambda$, then one has

$$Atb = \frac{\omega Y_1}{(\mu+\alpha+\omega)} - \frac{(\mu+\alpha)}{\lambda}.$$

Now, from $\beta Y_1(1 - Y_1 - A - Atb) - (\mu+\omega)Y_1 = 0$, one gets either $Y_1 = 0$, thus

$$Atb = -\frac{(\mu+\alpha)}{\lambda}$$

or

$$Y_1 = \left[\frac{\{\lambda[\beta-(\mu+\omega)] - \beta\theta\}(\mu+\alpha+\theta)}{\lambda\beta(\omega+\mu+\alpha+\theta)}\right],$$

thus

$$Atb = \frac{\lambda\omega[\beta-(\mu+\omega)] - \beta\omega\theta}{\lambda\beta(\omega+\mu+\alpha+\theta)} - \frac{(\mu+\alpha)}{\lambda}.$$

Then, one has two non-trivial equilibrium points for this case, which are:

1. $P_2 = (X_1, 0, 0, 0, 0, A, Atb)$, where

$$X_1 = \frac{1}{R_0^{\mathrm{HIV}}}; \quad A = \frac{(\mu+\alpha+\theta)}{\lambda} \quad \text{and} \quad Atb = -\frac{(\mu+\alpha)}{\lambda}, \tag{9}$$

which is not biologically feasible, since Atb is negative.

2. $P_3 = (X_1, 0, 0, Y_1, 0, A, Atb)$, where

$$\begin{aligned} X_1 &= \frac{1}{R_0^{\mathrm{HIV}}} \\ Y_1 &= \left[\frac{\lambda[\beta - (\mu+\omega)] - \beta\theta}{\lambda\beta}\right]\frac{(\mu+\alpha+\theta)}{(\omega+\mu+\alpha+\theta)} \\ &= \left[\frac{R_0^{\mathrm{HIV}}-1}{R_0^{\mathrm{HIV}}} - \frac{\theta}{\lambda}\right]\frac{(\mu+\alpha+\theta)}{(\mu+\alpha+\omega+\theta)} \\ A &= \frac{(\mu+\alpha+\theta)}{\lambda} \\ Atb &= \frac{\lambda\omega[\beta-(\mu+\omega)] - \beta\omega\theta}{\lambda\beta(\omega+\mu+\alpha+\theta)} - \frac{(\mu+\alpha)}{\lambda} \\ &= \frac{\omega(R_0^{\mathrm{HIV}}-1)}{(\mu+\alpha+\omega+\theta)R_0^{\mathrm{HIV}}} - \left[\frac{\theta_\omega}{\lambda(\mu+\alpha+\omega+\theta)} + \frac{(\mu+\alpha)}{\lambda}\right], \end{aligned} \tag{10}$$

and its biological feasibility depends upon the both values of λ and β. If

$$\lambda > \frac{\theta\beta}{\beta-(\mu+\omega)} = \frac{\theta R_0^{\mathrm{HIV}}}{R_0^{\mathrm{HIV}}-1} = \lambda_1^* \quad \text{and}$$

$$\lambda > \lambda_1^* + \frac{R_0^{\mathrm{HIV}}(\omega+\mu+\alpha+\theta)(\mu+\alpha)}{(R_0^{\mathrm{HIV}}-1)\omega} = \lambda_2^*$$

then one has $Y_1 > 0$ and $Atb > 0$, respectively, since $R_0^{\mathrm{HIV}} > 1$ and β is sufficiently large for each λ. The value of A is assured to be positive because all transition rates of the model are non-negative. Hence P_3 is biologically feasible for $\lambda > \lambda_2^*$ and $R_0^{\mathrm{HIV}} > 1$. It is easy to very that $\lambda_2^* = \lambda_1(\beta)$, where $\lambda_1(\beta)$ is defined by (13). ■

Biotheorem 3 *Assume that the prevalence of TB is remaining endemic while the prevalence of AIDS is vanishing in the community, after control interventions for AIDS were taken. In mathematical terms these assumptions mean* $R_0^{\mathrm{TB}} > 1$ *and* $A = 0$. *Then there is a single non-trivial and biologically feasible equilibrium point given by* $P_4 = (X_1, X_2, Tb, 0, 0, 0, 0)$.

Proof The proof is analogous to the proof of Biotheorem 1. In our system of coupled non-linear differential equations denoted by MATB, let us take $A = 0$. The equilibrium point of such a system are given by equations:

$$\begin{cases} \lambda\, Tb(1 - X_2 - Tb - Y_1 - Y_2 - Atb) - \beta\, X_2(Y_1 + Y_2) \\ \quad +\rho\, Tb - (\sigma+\mu)\, X_2 = 0 \\ \sigma\, X_2 - \beta\, Tb\,(Y_1 + Y_2) - (\rho+\mu+\theta)\, Tb = 0 \\ \beta\,(Y_1 + Y_2)(1 - X_2 - Tb - Y_1 - Y_2 - Atb) - \lambda\, Y_1\, Tb - (\mu+\omega) Y_1 = 0 \\ \beta\, X_2(Y_1 + Y_2) + \lambda\, Y_1\, Tb - (\xi+\mu)\, Y_2 = 0 \\ \omega\, Y_1 = 0 \\ \xi\, Y_2 + \beta\, Tb\,(Y_1 + Y_2) - (\mu+\alpha+\theta)\, Atb = 0. \end{cases}$$

From the above, one gets as one possibility that all state variables, but X_2 and Tb, vanish. Thus, we have the non-trivial equilibrium point given by $P_4 = (X_1, X_2, Tb, 0, 0, 0, 0)$ and its coordinates are given by

$$\begin{aligned} X_1 &= \frac{1}{R_0^{\mathrm{TB}}} \\ X_2 &= \frac{(\rho+\mu+\theta)}{\sigma} Tb = \frac{(\rho+\mu+\theta)(R_0^{\mathrm{TB}}-1)}{(\sigma+\rho+\mu+\theta)R_0^{\mathrm{TB}}} \\ Tb &= \frac{\lambda\sigma - \sigma(\mu+\theta) - \mu(\rho+\mu+\theta)}{\lambda(\sigma+\rho+\mu+\theta)} = \frac{\sigma(R_0^{\mathrm{TB}}-1)}{(\sigma+\rho+\mu+\theta)R_0^{\mathrm{TB}}}. \end{aligned} \tag{11}$$

Finally, both X_2 and Tb are positive, since $R_0^{\mathrm{TB}} > 1$ (λ is assumed from the onset to be over threshold). Hence this point $P_4 = (X_1, X_2, Tb, 0, 0, 0, 0)$ is biologically feasible. ■

2.3. Comments

We supposed that the prevalence of AIDS or TB decreases and vanishes after control interventions are taken. With that biological simplification, Biotheorems 2 and 3 enable us to determine the non-trivial equilibrium points. Similar analysis show that for any other subpopulation (or state variable) that is submitted to this biological simplification, one obtains the critical points of the Biotheorems above, plus three points which will be discussed below. We will denote this technique as the control technique. According to our control technique when the number of new cases of the HIV^+ individuals without MTB infection (Y_1) or the number of new cases of the HIV^+ individuals with MTB infection (Y_2) declines and vanishes, one gets the points $P_5 = (X_1, X_2, Tb, 0, 0, A, Atb)$ or $P_6 = (X_1, X_2, Tb, Y_1, 0, A, Atb)$, respectively, in addition to the critical points obtained. However, these equilibrium points are not biologically feasible.

We can also observe that $Tb = 0$ gives $P_3 = (X_1, 0, 0, Y_1, 0, A, Atb)$ because of our assumption: the individuals with AIDS (A and Atb) are considered so ill that they are transferred to the Center for Infectious Diseases to receive treatment. Thus, they do not transmit HIV infection, but the AIDS individuals with TB (Atb) transmit MTB infection to AIDS individuals without TB (A), showing that TB is an opportunist infection of AIDS. The only equilibrium point found numerically with all positive state variables is $P_7 = (X_1, X_2, Tb, Y_1, Y_2, A, Atb)$. This point is feasible only when HIV and MTB transmission coefficients are over thresholds; as it should be expected. It is important to stress that all the other cases (e.g., $X_2 = 0$, $Atb = 0$, $X_2 = Tb = 0$, etc.) lead up to the non-trivial equilibrium points obtained from Biotheorems above.

3. STABILITY ANALYSIS OF THE EQUILIBRIUM POINTS OF THE MODEL

We are now interested in studying this model in situations where the diseases can be established in the population and for these we have to determine the values of the threshold for the both transmission coefficients. Therefore, our purpose is to address the following question: if the diseases remain endemic in the community, that is, if

$R_0^{\mathrm{HIV}} > 1$ and $R_0^{\mathrm{TB}} > 1$, is there any relation between β and λ so that we will have stable or unstable non-trivial equilibrium points? We will answer this question by providing a summary of the stability conditions for each of the equilibrium points found. Regardless of their biological feasibility, we have the following:

BIOTHEOREM 4 *Under the same assumptions given by Biotheorem* 1, 2 *and* 3, *the c given below are the necessary and sufficient to warrant stability of the point under consideration:*

1. $P_\phi = (X_1, 0, 0, 0, 0, 0, 0)$ *is locally asymptotically stable if*

$$R_0^{\mathrm{HIV}} < 1 \quad \text{and} \quad R_0^{\mathrm{TB}} < 1. \tag{12}$$

2. $P_1 = (X_1, 0, 0, Y_1, 0, A, 0)$ *is locally asymptotically stable if for* $R_0^{\mathrm{HIV}} > 1$,

$$\begin{aligned} &\lambda < \frac{(\mu+\alpha+\theta)\beta(\mu+\alpha+\omega)}{\omega[\beta-(\mu+\omega)]} = \frac{(\mu+\alpha+\theta)(\mu+\alpha+\omega)R_0^{\mathrm{HIV}}}{\omega[R_0^{\mathrm{HIV}}-1]} \equiv \lambda_1(\beta) \\ &\textit{and} \\ &\lambda < \beta\left[\frac{\beta\, Y_1(\sigma+2\mu+\rho+\theta)+\beta^2 Y_1^2+\sigma(\mu+\theta)+\mu(\rho+\mu+\theta)}{\sigma(\mu+\omega)}\right] \equiv \lambda_2(\beta). \end{aligned} \tag{13}$$

3. $P_2 = (X_1, 0, 0, 0, 0, A, Atb)$ *is always unstable.*
4. $P_3 = (X_1, 0, 0, Y_1, 0, A, Atb)$ *is locally asymptotically stable if for* $R_0^{\mathrm{HIV}} > 1$,

$$\lambda_2(\beta) > \lambda > \lambda_1(\beta). \tag{14}$$

5. $P_4 = (X_1, X_2, Tb, 0, 0, 0, 0)$ *is locally asymptotically stable if for* $R_0^{\mathrm{TB}} > 1$,

$$\beta < \frac{-[\lambda\, Tb + (\mu+\omega)]\,(\xi+\mu)}{(\xi+\mu)\,(Tb-1) + X_2(\xi-\omega) + \lambda\, Tb\,(Tb-1)} \equiv \beta_2(\lambda). \tag{15}$$

6. $P_5 = (X_1, X_2, Tb, 0, 0, A, Atb)$ *is always unstable.*
7. $P_6 = (X_1, X_2, Tb, Y_1, 0, A, Atb)$ *is always unstable.*
8. $P_7 = (X_1, X_2, Tb, Y_1, Y_2, A, Atb)$ *is locally asymptotically stable when the values of* β *and* λ *are such that they do not satisfy the inequalities* (12), (13), (14) *and* (15) *simultaneously.*

Proof The results are obtained by linearizing the MATB model around each of the seven (P_ϕ, P_1, P_2, P_3, P_4, P_5 and P_6) equilibrium points. Note that the point P_7 is the only equilibrium point for which we are not able to obtain the analytical stability condition because we found its coordinates numerically. So its stability was only numerically determined.

We have just showed the proof for P_ϕ by Biotheorem 1. Now, we intend to show the proof for the point P_1; the calculations for the remaining points are similar.

Calculating the Jacobian matrix of the system (3) at the non-trivial equilibrium point P_1 we obtain the following characteristic polynomial $P(r_i)$, where r_i $(i=1,\ldots,6)$ is the notation for the eigenvalues:

$$\begin{aligned} P(r_i) = {} & \{\{[-\beta Y_1 - (\sigma+\mu)] - r_1\}\{[-\beta Y_1 - (\rho+\mu+\theta)] - r_2\} \\ & \times [-(\xi+\mu) - r_4][\lambda A - (\mu+\alpha+\theta) - r_6]\det \mathbf{M}\} \\ & - \{\sigma[\lambda - \lambda(Y_1+A)+\rho][-(\xi+\mu) - r_4] \\ & \times [\lambda A - (\mu+\alpha+\theta) - r_6]\det \mathbf{M}\} = 0 \end{aligned} \tag{16}$$

and the matrix $\mathbf{M}$ is defined as follows:

$$\mathbf{M} = \begin{bmatrix} \beta - \beta(2Y_1 + A) - (\mu+\omega) - r_3 & -\beta Y_1 \\ \omega & -(\mu+\alpha) - r_5 \end{bmatrix}.$$

After some simplifications the Eq. (16) becomes

$$\begin{aligned} P(r_i) = {} & [-(\xi+\mu) - r_4]\{[\lambda A - (\mu+\alpha+\theta)] - r_6\}\det \mathbf{M} \\ & \times \{\{[-\beta Y_1 - (\rho+\mu+\theta)] - r_2\}\{[-\beta Y_1 - (\sigma+\mu)] - r_1\} \\ & - \{\sigma[\lambda - \lambda(Y_1+A)+\rho]\}\} = 0. \end{aligned} \tag{17}$$

For the stability of the steady state P_1, we now find the roots of the characteristic polynomial by solving (17), that is,

(a) $-(\xi+\mu) - r_4 = 0 \Longrightarrow r_4 = -(\xi+\mu) < 0.$

(b) $[\lambda A - (\mu+\alpha+\theta)] - r_6 = 0 \Longrightarrow r_6 = \lambda A - (\mu+\alpha+\theta)$ and

$$r_6 < 0 \Longleftrightarrow \lambda < \frac{\beta(\mu+\alpha+\theta)(\mu+\alpha+\omega)}{\omega[\beta - (\mu+\omega)]} = \lambda_1(\beta). \tag{18}$$

(c) $\det \mathbf{M} = 0.$

We simplify this analysis by setting

$$\mathbf{M} = \begin{bmatrix} \beta - \beta(2Y_1 + A) - (\mu+\omega) & -\beta Y_1 \\ \omega & -(\mu+\alpha) \end{bmatrix},$$

where *trace* $\mathbf{M} < 0$ if $\beta > -\alpha$ and this inequality is always satisfied, and $\det \mathbf{M} > 0$ if $R_0^{\mathrm{HIV}} > 1$.

Thus, when $R_0^{\mathrm{HIV}} > 1$, the eigenvalues (r_3 and r_5) of the characteristic equation associated to matrix $\mathbf{M}$ are both negative (if real) or have negative real part (if complex).

(d) Now, by solving

$$\begin{aligned} & - \{[\beta Y_1 + \rho + \mu + \theta] + r_2\}\{[\beta Y_1 + \sigma + \mu] + r_1\} \\ & - \{\sigma[\lambda - \lambda(Y_1 + A) + \rho]\} = 0 \end{aligned}$$

we obtain the following characteristic polynomial:

$$r^2 + (2\beta Y_1 + \sigma + 2\mu + \rho + \theta)r + \beta Y_1(\sigma + 2\mu + \rho + \theta) + (\beta Y_1)^2 + \sigma(\mu + \theta) + \mu(\rho + \mu + \theta) - \lambda\sigma(1 - Y_1 - A) = 0.$$

The eigenvalues (r_1 and r_2) of this characteristic polynomial are both negative (if real) or have negative real part (if complex) when

$$\lambda < \frac{\beta\left[\beta Y_1(\sigma + 2\mu + \rho + \theta) + \beta^2 Y_1^2 + \sigma(\mu + \theta) + \mu(\rho + \mu + \theta)\right]}{\sigma(\mu + \omega)} = \lambda_2(\beta). \qquad (19)$$

Thus, for $R_0^{\mathrm{HIV}} > 1$, we conclude that P_1 is locally asymptotically stable if (18) and (19) are simultaneously satisfied. That is, P_1 is locally asymptotically stable if $\lambda < \lambda_1(\beta)$ and $\lambda < \lambda_2(\beta)$ for $R_0^{\mathrm{HIV}} > 1$, with $\lambda_1(\beta)$ and $\lambda_2(\beta)$ defined by (13).

3.1. Comments

From results obtained through linearizing the MATB model around each of the seven (P_ϕ, P_1, P_2, P_3, P_4, P_5 and P_6) equilibrium points, we are now able to establish the following: the only stable non-trivial equilibrium points are those that are biologically feasible.

Besides that, we can also observed that the stability conditions for each of the equilibrium points given by the Biotheorem 4 depend on the both transmission coefficients for HIV and for MTB (β and λ) which must be estimated. The other parameters were evaluated from the literature and we considered these values as follows: $\rho = 0.5$, $\sigma = 0.05$, $\mu = 0.10$, $\omega = 0.10$, $\xi = 0.20$, $\theta = 0.05$, $\alpha = 0.33$ (in year^{-1}).

In this way, different basins of attractions of these critical points can be found in the space of parameters λ and β, which are defined as follows:

1. The basin $R_\phi = \{(\beta, \lambda): \beta < \beta_t \text{ and } \lambda < \lambda_t\}$, where P_ϕ is stable. Biologically, R_ϕ is the basin where both diseases die out in the community.
2. The basin $R_1 = \{(\beta, \lambda): \beta > \beta_t, \lambda < \lambda_1(\beta) \text{ and } \lambda < \lambda_2(\beta)\}$, where P_1 is stable. Biologically, R_1 is the basin where the HIV infection progress to AIDS disease.
3. The basin $R_3 = \{(\beta, \lambda): \beta > \beta_t, \lambda > \lambda_1(\beta) \text{ and } \lambda < \lambda_2(\beta)\}$, where P_3 is stable. Biologically, R_3 is the basin where the HIV infection progress to AIDS with TB disease.
4. The basin $R_4 = \{(\beta, \lambda): \lambda > \lambda_t \text{ and } \beta < \beta_2(\lambda)\}$ where P_4 is stable. Biologically, R_4 is the basin where the MTB infection progress to TB disease.
5. The basin $R_7 = \{(\beta, \lambda): \beta > \beta_t, \lambda > \lambda_t, \beta > \beta_2(\lambda) \text{ and } \lambda > \lambda_2(\beta)\}$, where there is a co-existence of the diseases, i.e., HIV and MTB infections progress to AIDS and TB diseases, respectively.
6. The basin $R_1R_4 = \{(\beta, \lambda): \beta > \beta_t, \lambda > \lambda_t, \beta < \beta_2(\lambda) \text{ and } \lambda < \lambda_2(\beta)\}$, where P_1 and P_4 are simultaneously stable.

These basins of attraction can be visualized, as shown in Fig. 1.

It is important to stress that the stable basins depend on the parameter values that were maintained constant during the analysis, because they are obtained from the literature. For different values of the parameters one obtains the same basins; however, their magnitude may be different from what is shown in Fig. 1.

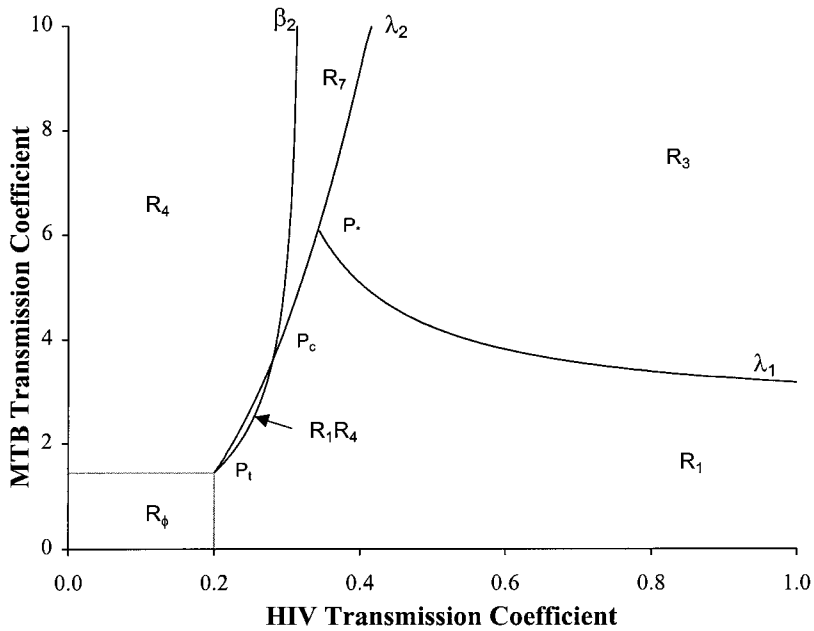

FIGURE 1 Basins of attractions of the equilibrium points of the MATB model, when β and λ are varied. $P_t = (\beta_t, \lambda_t) = (0.2, 1.45)$; $P_c = (\beta_c, \lambda_c) = (0.280168, 3.60756)$; $P^* = (\beta^*, \lambda^*) = (0.342581, 6.1125)$.

We observed that in the basins R_ϕ, $(R_1 - R_1R_4)$, R_3, $(R_4 - R_1R_4)$ and R_7, the stability of each equilibrium point does not depend on the initial conditions of the MATB model. In the R_1R_4 basin, where the P_1 and P_4 points are stable, the MATB depends on the initial conditions (these observations were tested numerically).

In the basins where the MATB does not depend on the initial conditions, for any values of the pair (β, λ) belonging to a determined basin of stability, only the corresponding point of this basin is stable. That is, if β and λ satisfy the conditions of $(R_1 - R_1R_4)$, we obtain P_1 stable and the other points, P_ϕ, P_3, P_4 and P_7 unstable.

In the basin R_1R_4 this does not occur. There are basins of attraction from the points P_1 and P_4 and, depending on the initial conditions, we can have in R_1R_4, P_1 or P_4 stable for the same values of β and λ. We also point out that only the points P_1 and P_4 can be stable in the basin R_1R_4 (Biotheorem 4) and that the existence of this basin is strongly dependent on the value of the parameter μ.

The curves which limit the basins of stability are generally conditions of bifurcation to the feasible equilibrium point. There is a change in the qualitative structure of the MATB when the parameters β and λ vary beyond their threshold values, keeping constant all other values. That is, the conditions stability of the trivial equilibrium point and the endemic basins are based on threshold values for β and λ. When these conditions are invalidated another steady state accepts stability. Therefore, they are transcritical bifurcation:

1. When $\beta < \beta_t$ and $\lambda < \lambda_t$, P_ϕ is asymptotically stable.
2. If $\beta > \beta_t$ and $\lambda < \lambda_t$, we have point P_1 asymptotically stable and P_ϕ unstable. The curve $C_1 = \{(\beta, \lambda): \beta = \beta_t, 0 \leq \lambda < \lambda_t\}$ determines the bifurcation condition from point P_ϕ to point P_1.

3. Similarly, if $\beta < \beta_t$ and $\lambda > \lambda_t$, we have point P_4 asymptotically stable and P_ϕ unstable. The curve $C_2 = \{(\beta, \lambda): \lambda = \lambda_t, 0 \leq \beta < \beta_t\}$ determines the bifurcation condition from point P_ϕ to point P_4.
4. If $\beta > \beta_t$ and $\lambda > \lambda_t$ we can have P_1, P_3, P_4 or P_7 asymptotically stable.

The curves:

$C_3 = \{(\beta, \lambda): \lambda(t) = \lambda_1(\beta)\}$ determines the bifurcation condition from point P_1 to point P_3.
$C_4 = \{(\beta, \lambda): \lambda(t) = \lambda_2(\beta)\}$ determines the bifurcation condition from point P_3 to point P_7; from point P_1 to point P_7 and from point P_1 to point P_4.
$C_5 = \{(\beta, \lambda): \beta(t) = \beta_2(\lambda)\}$ determines the bifurcation condition from point P_4 to points P_7 or P_4 and P_1.

The simulations show that over the curves C_1 and C_2 (the boundaries of the R_ϕ), in the neighborhood of the C_1 and C_2 and at the point $P_t = (\beta_t, \lambda_t)$ the MATB model depends on the initial conditions. For $\beta = \beta_t$, the stability conditions for the point P_1 given by (13) are not defined. Similarly, for $\lambda = \lambda_t$, the stability conditions for the point P_4 given by (15) are not defined. Besides that, for $\beta = \beta_t$ and $\lambda = \lambda_t$, the coordinates of the both P_1 and P_4 are null; thus $P_1 = P_4 = P_\phi$. From stability analysis (Biotheorem 4) we also observed that for $\beta = \beta_t$ and/or $\lambda = \lambda_t$, there are two/one null eigenvalues. Therefore, we have no information about the stability of P_ϕ at the boundary of the R_ϕ. However, we know that the point P_ϕ is a bifurcation point and depending on the initial conditions of the MATB model at the neighborhood $\mathcal{V}(P_\phi)$, we can have P_ϕ, P_1 or P_4 stable.

A two-parameter bifurcation diagram is shown in Fig. 1. If either parameters, β or λ, involved are varied, they each lead to a similar transcritical bifurcation scheme from one to another equilibrium point.

4. AN APPLICATION OF THE MODEL

On the previous sections our analytical study of the model (1) was performed to determine the basins of stability of HIV and MTB infections on a large range of the variation of the transmission coefficients for both diseases. Now, based on the observations done by Ferreira *et al.* [3] in followed up female inmates, we assess these transmission coefficients.

The field experiment carried out by Ferreira *et al.* presents the following features: the study participants, included women who were already incarcerated at the beginning of the study period and women admitted during the period of study, were interviewed and examined; during the period of study the symptomatic AIDS inmates were transferred to the Hospital for Infectious Diseases and AIDS; the TB disease inmates could transmit MTB infection during the time-lag of several days before their diagnoses and transfer to the Hospital for Infectious Diseases and AIDS and there were recruitment rates in the X_1, X_2, Y_1 and Y_2 compartments. However, there were not recruitment rates in the Tb, A and Atb compartments, since during the follow-up period the admitted prisoners with clinical signs and symptoms of diseases were transferred to the Hospital for Infectious Diseases and AIDS; and the mortality rate μ associated to the population model is now considered as the release rate, because

of female inmates who did not die during the study period, but were released after some period of time. Therefore, the modified model is given by the following elements of the space function $\dot{\mathbf{Z}} = \mathbf{F}(\mathbf{Z})$, where $\mathbf{Z}$ is the space of dynamics variable given by a vector of 7-elements $\mathbf{Z} = [X_1\ X_2\ Tb\ Y_1\ \ Y_2\ A\ Atb]^T$,

$$\begin{cases} F_1(\mathbf{Z}) = \phi_1 - \beta_1(Y_1 + Y_2)X_1 - \beta_2 TbX_1 - \mu X_1 \\ F_2(\mathbf{Z}) = \phi_2 - \beta_1(Y_1 + Y_2)X_2 + \beta_2 TbX_1 + \rho Tb - (\sigma + \mu)X_2 \\ F_3(\mathbf{Z}) = \sigma X_2 - \beta_1(Y_1 + Y_2)Tb - (\rho + \theta + \mu)Tb \\ F_4(\mathbf{Z}) = \phi_3 + \beta_1(Y_1 + Y_2)X_1 - \beta_2 Tb Y_1 - (\omega + \mu)Y_1 \\ F_5(\mathbf{Z}) = \phi_4 + \beta_1(Y_1 + Y_2)X_2 + \beta_2 Tb Y_1 - (\xi + \mu)Y_2 \\ F_6(\mathbf{Z}) = \omega Y_1 - \beta_2\, Atb\, A - (\alpha + \mu)A \\ F_7(\mathbf{Z}) = \xi Y_2 + \beta_2\, Atb\, A - (\alpha + \theta + \mu)\, Atb + \beta_1(Y_1 + Y_2)Tb. \end{cases} \tag{20}$$

On the preceding section we dealt with the fractions of individuals in each compartment. We are now considering restricted female inmates and we take into account the number of individuals, $N(t)$, which is very low. Even so we are retaining the very strong assumption of the both infections occurring in a homogeneously mixed population. Besides that, the total population is no longer a constant.

The above modified system (20) has at least a positive equilibrium point $P^*_{\phi_i} = (X_1^*, X_2^*, Tb^*, Y_1^*, Y_2^*, A^*, Atb^*)$. Letting $\mathbf{F}(\mathbf{Z}) = 0$, we get

1. $\mathbf{F}_1(\mathbf{Z}) = 0 \Leftrightarrow [\beta_1(Y_1 + Y_2) + \beta_2 Tb + \mu]X_1 = \phi_1$. If $X_1 = 0$ then $\phi_1 = 0$; a contradiction. Hence, $X_1 > 0$.
2. $\mathbf{F}_3(\mathbf{Z}) = 0 \Leftrightarrow Tb = \sigma X_2/[\beta_1(Y_1 + Y_2) + (\rho + \theta + \mu)]$ and
3. $\mathbf{F}_2(\mathbf{Z}) = 0 \Leftrightarrow [\beta_1(Y_1 + Y_2) + (\sigma + \mu) - ((\beta_2 X_1 + \rho)\sigma/[\beta_1(Y_1 + Y_2) + (\rho + \theta + \mu))]X_2 = \phi_2$. If $X_2 = 0$ then $\phi_2 = 0$; a contradiction. Hence, $X_2 > 0$ and $Tb > 0$.
4. $\mathbf{F}_4(\mathbf{Z}) = 0 \Leftrightarrow [-\beta_1 X_1 + \beta_2 Tb + (\omega + \mu)]Y_1 = \phi_3 + \beta_1 X_1 Y_2 > 0 \Rightarrow \quad Y_1 \neq 0$. If $\beta_2 Tb + (\omega + \mu) < \beta_1 X_1 \Rightarrow Y_1 < 0$, that is not biologically feasible. Thus, $\beta_2 Tb + (\omega + \mu) > \beta_1 X_1$ and $Y_1 > 0$.
5. $\mathbf{F}_5(\mathbf{Z}) = 0 \Leftrightarrow [-\beta_1 X_2 + (\xi + \mu)]Y_2 = \phi_4 + [\beta_2 Tb + \beta_1 X_2]Y_1 > 0 \Rightarrow \quad Y_2 \neq 0$. If $(\xi + \mu) < \beta_1 X_2 \Rightarrow Y_2 < 0$, that is not biologically feasible. Hence, $(\xi + \mu) > \beta_1 X_2$ and $Y_2 > 0$.
6. $\mathbf{F}_6(\mathbf{Z}) = 0 \Leftrightarrow [\beta_2 Atb + (\alpha + \mu)]A = \omega Y_1 > 0 \Rightarrow A > 0$.
7. $\mathbf{F}_7(\mathbf{Z}) = 0 \Leftrightarrow [-\beta_2 A + (\alpha + \theta + \mu)]Atb = \xi Y_2 + \beta_1(Y_1 + Y_2)Tb > 0 \ \Rightarrow \ Atb \neq 0$. If $(\alpha + \theta + \mu) < \beta_2 A \Rightarrow Atb < 0$, which is not biologically feasible. Thus, $(\alpha + \theta + \mu) > \beta_2 A \Rightarrow Atb > 0$.

Therefore, the presence of the four recruitment rates ϕ_1, ϕ_2, ϕ_3 and ϕ_4 leads to the positive equilibrium point, which must be always stable on all ranges of the variations of β_1 and β_2. Next, we will deal with the assessment of both transmission coefficients.

4.1. Estimation of the Transmission Coefficients

We can now observe that the system (20) allows the co-existence of AIDS and TB when $\beta_1 = \beta_2 = 0$. That is, the steady state $P^*_{\phi_i} = (X_1^*, X_2^*, Tb^*, Y_1^*, Y_2^*, A^*, Atb^*)$ is given by

$X_1^* = \phi_1/\mu$, $X_2^* = ((\rho+\mu+\theta)/\sigma)(\phi_2/\lambda_t)$, $Tb^* = \phi_2/\lambda_t$, $Y_1^* = \phi_3/\beta_t$, $Y_2^* = \phi_4/(\xi+\mu)$, $A^* = \omega\phi_3/((\alpha+\mu)\beta_t)$, and $Atb^* = \xi\phi_4/((\xi+\mu)(\mu+\alpha+\theta))$, with λ_t and β_t defined by Eq. (6). Note that this non-trivial equilibrium point is always biologically viable.

The Jacobian matrix of the system (20) at the non-trivial equilibrium point $P_{\phi_i}^*$ gives the following five eigenvalues: $\lambda_1 = -\mu$; $\lambda_2 = -(\mu+\omega)$; $\lambda_3 = -(\mu+\alpha)$; $\lambda_4 = -(\mu+\xi)$; $\lambda_5 = -(\mu+\alpha+\theta)$, while the other two eigenvalues are given by the roots of the following characteristic equation:

$$\lambda^2 + (\rho+\sigma+\theta+2\mu)\lambda + [\mu(\rho+\theta+\mu) + \sigma(\theta+\mu)] = 0.$$

According to Routh–Hurwitz criterion the eigenvalues of this equation have negative real part [2]. Thus, the equilibrium point $P_{\phi_i}^*$ is locally asymptotically stable and consequently, both diseases can be maintained in this community by the recruitment rates, even though $\beta_1 = \beta_2 = 0$.

Our purpose is to address the following question: if the diseases are able to become established in the female inmates community even though there is no transmission, is there an increased incidence and prevalence of infections or diseases due to recruitment rates? We will answer this question by estimating the transmission coefficients β_1 and β_2 in this community.

Ferreira *et al.* [3] carried out the study at the Female Penitentiary of the State of São Paulo during a 14-month period (October 1992 to November 1993). The sample consisted of incarcerated women at the beginning of the study ($n = 234$) plus those admitted during the period of the study ($n = 116$), in a total of 350 followed up women inmates.

The follow-up period (defined as the period between the initial date of incarceration and the end of the follow-up period) was in four times; $t = 0$, 6, 12 and 14 months. In each time of observation all individuals were screened by clinical observations and the number of recruited individuals was registered. In Table I we present the number of individuals discriminated by their health status and the observed recruitment rates.

We performed the estimation of transmission coefficients among women inmates in the Female Penitentiary of the State of São Paulo by considering four sequential times and three observable classes (X_2, Y_1 and Y_2). The number of individuals of the other classes were also collected at the beginning ($t = 0$) of the study period: $X_1 = 93$, $Tb = 0$, $A = 1$ and $Atb = 6$. The study period was also characterized by the following rates (year^{-1}): $\mu = 0.4$, $\theta = 0$ and $\alpha = 12.0$ [3]. The other rates (in year^{-1}) are: $\sigma = 4.0$, $\rho = 6.5$, $\omega = 0.25$, $\xi = 0.5$ [6].

Thus, the transmission coefficients are assessed [10] based on the number of cases observed and the recruitment rates given in Table I. In order to do this, we minimize

TABLE I Observed number of cases at the Female Penitentiary of the State of São Paulo

t (months)	*Number of cases,* $\mathbf{Z}(\text{obs}_i)$				*Input,* ϕ_i		
	0	*6*	*12*	*14*	*0*	*6*	*12*
X_1					34	90	12
X_2	84	83	99	105	42	2	6
Y_1	21	13	18	28	20	26	0
Y_2	18	22	32	35	12	0	6

the chi-square defined as

$$\chi^2 = \sum_{i=1}^{n} [\{\mathbf{Z}(t_i) - \mathbf{Z}(\text{obs}_i)\}\mathbf{D}]^2, \tag{21}$$

where $n = 1, 2, 3, 4$ is the number of observation times, $\mathbf{Z}(t_i)$ is the state variables of the system (20), $\mathbf{Z}$ (obs_i) is the number of cases observed (Table I), $\mathbf{D}$ is 7×7 diagonal matrix, whose diagonal elements [0 1 0 1 1 0 0] depend on the number of observed state variables.

By the non-linear least square estimation method [1], setting $\Omega = [\beta_1\ \beta_2]^T$ as the parameters space, the least square estimator must satisfy

$$\frac{1}{2}\frac{d\chi^2}{d\Omega} = \sum_{i=1}^{n} [\{\mathbf{Z}(t_i) - \mathbf{Z}(\text{obs}_i)\}\mathbf{D}]\frac{\partial \mathbf{Z}(t_i)}{\partial \Omega}\mathbf{D} = 0 \tag{22}$$

and

$$\frac{1}{2}\frac{d^2\chi^2}{d\Omega^2} \simeq \sum_{i=1}^{n} \left[\frac{\partial \mathbf{Z}(t_i)}{\partial \Omega}\mathbf{D}\right]^2 > 0. \tag{23}$$

This inequality comes out by neglecting the second partial derivative of the state variables with respect to the parameters. We approximated the second derivative because the other term $[\{\mathbf{Z}(t_i) - \mathbf{Z}(\text{obs}_i)\}\mathbf{D}](\partial^2 \mathbf{Z}(t_i)/\partial\Omega^2)\,\mathbf{D}$ is negligible compared to the term retained in the Eq. (23) [8].

To solve the algebraic system of Eqs. (22) we applied the Levenberg–Marquardt method by using the approximation in the second derivative given by Eq. (23), instead of Newton–Raphson method. The derivatives of the state variables with respect to the parameters space are calculated by

$$\frac{\partial \mathbf{Z}}{\partial \Omega} = \left[\frac{\partial \mathbf{F}(\mathbf{Z})}{\partial \mathbf{Z}}\right]^{-1}\frac{\partial \mathbf{F}(\mathbf{Z})}{\partial \Omega}, \tag{24}$$

where $\partial\mathbf{F}(\mathbf{Z})/\partial\mathbf{Z}$ is the Jacobian matrix and $\partial\mathbf{F}(\mathbf{Z})/\partial\Omega$ is the sensitivity matrix. We applied fourth order stepsize controlled Runge–Kutta method to evaluated numerical calculation of the system (20). The set of parameters $\hat{\Omega}$ which satisfies the conditions (22) and (23) are the searched values.

In Table II we present the estimated transmission coefficients, that are based on data collected at Female Penitentiary of São Paulo, Brazil [3].

4.2. Comments

The HIV transmission coefficient is null in this approach. That is, there is no increase in the incidence of HIV infection or AIDS disease among female inmates. The absence of

TABLE II The fitted transmission coefficients considering three compartments observed

Parameters	*Fitted values*
β_1	0.00 ± 0.02
β_2	0.175 ± 0.0002
χ^2	2278.34

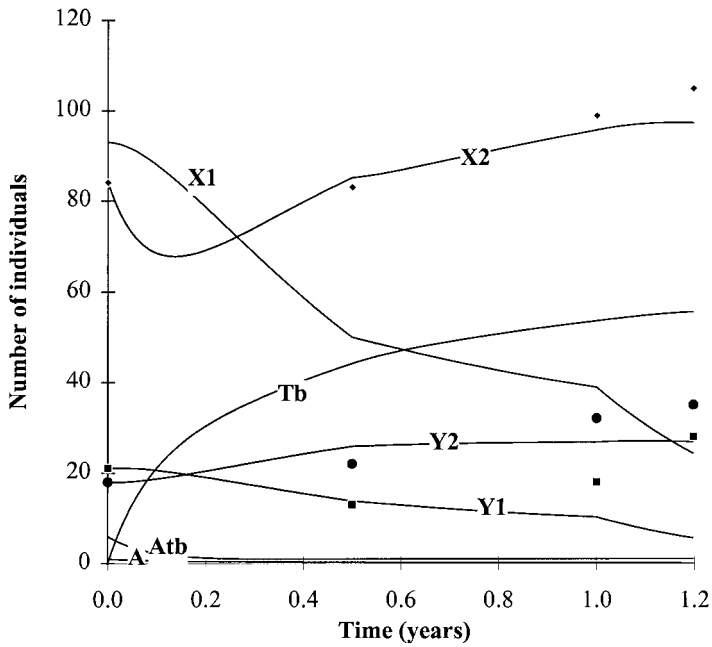

FIGURE 2 The dynamic behavior of the seven state variables of the model considering the fitted transmission coefficients based on three observable classes.

transmission among them can be explained by rigorous watchfulness that avoids the HIV transmission routes, that is, it aborts any attempts of intravenous drug usage and it does not permit the sexual intercourse during the visiting. In spite of that, since the admitted prisoners may serve as a source of cases to the prison, an increase in the prevalence of HIV infection may be observed and HIV infection is maintained among them. Conversely, TB is a directly transmitted air-borne infection. The women inmates are together during meals, sunbathing or walking, owing to which an increased incidence of MTB infection may also occur.

The estimated transmission coefficients suggest that the watchfulness can avoid the new cases of HIV infection, but not new cases of MTB infection. That is, as Ferreira *et al.* [3] characterized in their follow up study, our estimation also characterizes an increased incidence of MTB infection and TB disease with a high prevalence of HIV infection in a female prison. Using the values of the estimated transmission coefficients, Fig. 2 shows the fitting.

5. DISCUSSION

The importance of the effects of opportunistic infections on the course of HIV are now being explored by mathematical models. In this paper we proposed to analyze a model which describes the dynamical interaction of co-infections in a closed community. Our major contribution consists in showing how we can determine the non-trivial equilibrium point through biological simplifications. That procedure was called control technique and it was made valid when we showed that the non-trivial stable equilibrium points are precisely the points which are feasible from a biological aspect. Also, we

noted that the analysis of the stability basins of MATB model is based on the parameters μ (natural mortality or remaining time in prison or in mental institution), β and λ. We made the sensitivity analysis of the parameters and through this analysis we observed that the parameters (μ, β, λ) are the most sensitive in the MATB model.

We point out that the basin R_1R_4 strongly depends on the value given to μ; this parameter is sensitive to all MATB model variables. From an epidemiological viewpoint, this is remarkably relevant as μ is the remaining time in prison for punishment or in the mental institution for treatment. It seems obvious that the longer the individual remains in a prison, for instance, the easier the disease transmission becomes. When β and λ belong to this basin there seems to exist a strong competition between AIDS and TB and the prevalence of one of the diseases must happen in the population depending on the MATB initial condition. It was shown that the necessary and sufficient condition for the existence of the basin R_1R_4 is that $\beta_c > \beta_t$ and $\lambda_c > \lambda_t$ (Fig. 1). There is a value μ^* such that $P_t(\beta_t(\mu^*), \lambda_t(\mu^*)) = P_c(\beta_c(\mu^*), \lambda_c(\mu^*))$. If $\mu \geq \mu^*$, the basin R_1R_4 vanishes. The coordinates of the point P_t grow with μ; the basin R_ϕ rises and the possibility of eradicating the diseases in the community (or prison) is proportional to the μ value.

Furthermore, the growth of μ provides a decrease in basin R_7 (where AIDS and TB co-exist), while basins R_1 and R_4 grow and R_3 decreases. In epidemiological terms it means that the shorter an individual stays in prison the smaller the possibility of the diseases co-existing. That is, there exists a strong negative interaction between the two infections in the host. So, depending on the values of the pair (β, λ) there exists a greater possibility of the TB prevalence or AIDS prevalence (the basins R_4 or R_1, respectively) or the eradication of the both diseases (the basin R_ϕ) than the co-existence of the diseases (the basin R_7).

According to Fig. 1, we can also observe that MTB infection, in some extent, could be a preventive factor of the insurgence of HIV infection, if the incidence and prevalence of HIV is low. However, once HIV infection is established in a community (i.e., high transmission coefficient and high prevalence), the presence of MTB infection worsens the clinical picture for HIV, restricting this infection among AIDS individuals. On the other hand, the presence of HIV, infection can activate MTB infection, even to very low values for the MTB transmission coefficient. For this reason, TB occurs among AIDS individuals and, differently to the first situation, the increase in the MTB transmission coefficient leads to the co-infection with TB disease.

The model that we have analysed in this paper is useful for understanding the importance of the effects of opportunistic infections on the course of HIV. For instance, TB seemed to have been controlled and eradicated in the developed countries. Nevertheless, in the last couple of decades the incidence of TB has been steadily growing. In the US in particular, the growth has been dramatic since 1984, and HIV is believed to be culprit. The Biotheorems 2, 3 and 4 show this fact. When HIV did not exist TB could be controlled (Biotheorems 3 and 4). However, we had an increased incidence of TB, because of, indeed, TB is an opportunistic infection on the course of HIV (Biotheorems 2 and 4). Besides that, we have also applied the methodology to assess the transmission coefficients for HIV and MTB infections. In order to estimate these parameters we introduced strong assumptions because a reliable estimation is obtained when we have data about all subpopulation. Even though, we may be assured that this methodology can be used straight to any population data relating to co-infection.

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