

Research Article

Global Stability of a SLIT TB Model with Staged Progression

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Because the latent period and the infectious period of tuberculosis (TB) are very long, it is not reasonable to consider the time as constant. So this paper formulates a mathematical model that divides the latent period and the infectious period into n -stages. For a general n -stage stage progression (SP) model with bilinear incidence, we analyze its dynamic behavior. First, we give the basic reproduction number R_0 . Moreover, if $R_0 \leq 1$, the disease-free equilibrium P_0 is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, the unique endemic equilibrium P^* is globally asymptotically stable and the disease persists at the endemic equilibrium.

1. Introduction

Tuberculosis (TB) is one of the oldest recorded diseases of mankind. It is an disease caused by the infection of bacterium *Mycobacterium tuberculosis*. The disease is most commonly transmitted from a person suffering from infectious (active) tuberculosis to other persons by infected droplets created when the person with active TB coughs or sneezes. Most infected people do not develop the progressive disease. When the first time after being infected with *Mycobacterium tuberculosis*, the individual generally will experience a latent phase. TB progresses through a long latent period and a long infectious period. For this case, the infection can vary greatly in time. The progression of a typical TB infection can take four weeks to several years before the development into active disease, and a few individuals directly become infectious without experiencing latency. Moreover, most infected people do not develop the active disease in his or her life. In the infectious period, individual differences lead to different course. The longest infectious period is several decades while the shortest maybe only a few months. Moreover, the treatment of TB has side effects (sometimes quite serious) and takes varying time depending on the other various factors such as nutritional status and/or access to decent medical care and living conditions [1]. The progression of a TB infection goes through several distinct stages. Similarly, HIV virus has the long incubation

and infectious periods (infection age, from 8 to 10 years). During the incubation period, the infectivity of infected people is varying depending on the time since infection. When symptom onset appears, AIDS population transmission rate depends on disease age (i.e., the time elapsed since the onset) [2]. Different from common infectious diseases, the time scale of TB or HIV/AIDS transmission is so long that demographic of the host population could affect transmission process. The classic compartmental models that postulate all the hosts are similar and imprecise to describe the spread of an infection. For explore the issue, many authors formulate staged progression (SP) models [1, 3–9] and delayed epidemic models [10]. In [5], the authors analyze a mathematical model for infectious diseases that progress through distinct stages within infected hosts and prove the global dynamics of the equilibria. Hyman et al. [4] created two SP models to show the impact of variations in infectiousness. In [10], the author formulate a delayed SIR epidemic model by introducing a latent period into susceptible and infectious individuals in incidence rate. Mathematical modeling has become an important tool in analyzing the epidemiological characteristics of infectious diseases and can provide useful control measures. In [11–18], several variants and generalizations of the Beverton CHolt model (standard time-invariant, time-varying parameterized, generalized model or modified generalized model) have been investigated at the levels of stability, cycle-oscillatory behavior, permanence, and control through the manipulation of the carrying capacity. De la Sen et al. studied the impact of vaccination for infectious diseases. This paper considers the latent period and the infectious period to formulate a n -stage SP model with bilinear incidence (based on the model in [3]).

To formulate an SP model, the host population is divided into the following epidemiological classes or subgroups: the susceptible compartment S ; the latent compartment L_i (infected but not infectious), whose members are in the i th stage of the disease progression, where $i = 1, 2, \dots, n$; the infectious compartment I_j , whose members are in the j th stage of the disease progression, where $j = 1, 2, \dots, m$; the treated compartment T . N denotes the total population. Here we assume that the latent period is averagely divided into n stages and the infectious period is averagely divided into m stages. We also assume that hosts in the treated compartment are noninfectious due to inactivity. Using Figure 1, we formulate the following model:

$$\begin{aligned}
 \frac{dS}{dt} &= \Lambda - \lambda S - dS, \\
 \frac{dL_1}{dt} &= \lambda S - (n\delta + d)L_1, \\
 \frac{dL_i}{dt} &= n\delta L_{i-1} - (n\delta + d)L_i, \quad i = 2, 3, \dots, n, \\
 \frac{dI_1}{dt} &= n\delta L_n - (m\gamma + \mu + d)I_1, \\
 \frac{dI_j}{dt} &= m\gamma I_{j-1} - (m\gamma + \mu + d)I_j, \quad j = 2, 3, \dots, m-1, \\
 \frac{dI_m}{dt} &= m\gamma I_{m-1} - (k + \mu + d)I_m, \\
 \frac{dT}{dt} &= kI_m - dT.
 \end{aligned} \tag{1.1}$$

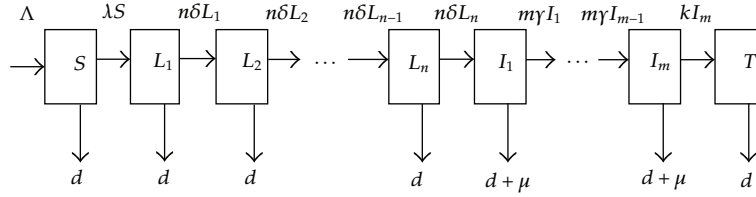


Figure 1: Transfer diagram.

The incidence form is λS , where the force of infection

$$\lambda = \sum_{j=1}^m \lambda_j I_j \quad (1.2)$$

is the bilinear incidence; $1/\delta$ is the incubation period, and $1/n\delta$ is the average incubation period from the i th stage to $(i+1)$ th stage, for $i = 1, 2, \dots, n-1$; $1/\gamma$ is the infectious period, and $1/m\gamma$ is the average infectious period from the j th stage to $(j+1)$ th stage, for $j = 1, 2, \dots, m-2$; Λ is the recruitment rate of susceptible; k is per-capita treatment rates, respectively; d is the per-capita natural death rate (and hence $1/d$ is an average lifespan of the healthy individuals in the population); μ is the per capita disease-induced death rate. $\Lambda, \delta, d, k, \gamma, \mu, \lambda$ are positive constants. Because in the model (1.1), the first $n + m + 1$ equations do not contain variable T , so dynamical behaviors of the model (1.1) are equivalent to the model (1.3).

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \lambda S - dS, \\ \frac{dL_1}{dt} &= \lambda S - (n\delta + d)L_1, \\ \frac{dL_i}{dt} &= n\delta L_{i-1} - (n\delta + d)L_i, \quad i = 2, 3, \dots, n, \\ \frac{dI_1}{dt} &= n\delta L_n - (m\gamma + \mu + d)I_1, \\ \frac{dI_j}{dt} &= m\gamma I_{j-1} - (m\gamma + \mu + d)I_j, \quad j = 2, 3, \dots, m-1, \\ \frac{dI_m}{dt} &= m\gamma I_{m-1} - (k + \mu + d)I_m. \end{aligned} \quad (1.3)$$

Let $N = S + \sum_{i=1}^n L_i + \sum_{j=1}^m I_j$, then using (1.3) we have

$$\frac{dN}{dt} = \Lambda - dN - \mu \sum_{j=1}^m I_j - kI_m. \quad (1.4)$$

This implies that $\lim_{t \rightarrow \infty} \sup N(t) \leq \Lambda/d$. Therefore, the model can be studied in the feasible region

$$\Gamma = \left\{ (S, L_1, \dots, L_n, I_1, \dots, I_m) \in R_{n+m+1}^+ : 0 \leq S + L_1 + \dots + L_n + I_1 + \dots + I_m \leq \frac{\Lambda}{d} \right\}. \quad (1.5)$$

2. The Basic Reproduction Number

The disease-free equilibrium is obtained by setting the right side of each of the $n + m + 1$ differential equations equal to zero in system (1.3).

If $I_j = 0, j = 1, \dots, m$, it is easy to deduce the disease-free equilibrium as follows:

$$P_0 = \left(\frac{\Lambda}{d}, 0, \dots, 0, 0, 0, \dots, 0 \right). \quad (2.1)$$

Next, we derive the basic reproductive number of (1.3) by the method of next-generation matrix formulated in [19].

Let $x = (L_1, L_2, \dots, L_n, I_1, I_2, \dots, I_m)^T$. Then the last $n + m$ equations of model (1.3) can be written as

$$x' = \mathcal{F}(x) - \mathcal{V}(x), \quad (2.2)$$

where

$$\mathcal{F}(x) = \begin{pmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}, \quad (2.3)$$

$$\mathcal{V}(x) = \begin{pmatrix} (n\delta + d)L_1 \\ -n\delta L_1 + (n\delta + d)L_2 \\ \vdots \\ -n\delta L_{n-1} + (n\delta + d)L_n \\ -n\delta L_n + (m\gamma + \mu + d)I_1 \\ -m\gamma I_1 + (m\gamma + \mu + d)I_2 \\ \vdots \\ -m\gamma I_{m-1} + (k + \mu + d)I_m \end{pmatrix}.$$

By calculating the Jacobian matrices of $\mathcal{F}(x)$ and $\mathcal{U}(x)$ at the disease-free equilibrium P_0 , we have

$$F = \begin{pmatrix} 0 & 0 & \cdots & 0 & \lambda_1 S & \lambda_2 S & \cdots & \lambda_m S \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \end{pmatrix}, \quad (2.4)$$

$$V = \begin{pmatrix} n\delta + d & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ -n\delta & n\delta + d & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & n\delta + d & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & -n\delta & m\gamma + \mu + d & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & -m\gamma & m\gamma + \mu + d & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & k + \mu + d \end{pmatrix}. \quad (2.5)$$

Let $I_{(n+m) \times (n+m)}$ be the identity matrix. Solving the matrix equation $VX = I_{(n+m) \times (n+m)}$, we obtain that $X = V^{-1}$ is a lower triangular matrix

$$V^{-1} = \begin{pmatrix} c_{11} & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ c_{21} & c_{22} & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ c_{n1} & c_{n2} & \cdots & c_{nn} & 0 & 0 & \cdots & 0 \\ c_{n+1,1} & c_{n+1,2} & \cdots & c_{n+1,n} & c_{n+1,n+1} & 0 & \cdots & 0 \\ c_{n+2,1} & c_{n+2,2} & \cdots & c_{n+2,n} & c_{n+2,n+1} & c_{n+2,n+2} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ c_{n+m,1} & c_{n+m,2} & \cdots & c_{n+m,n} & c_{n+m,n+1} & c_{n+m,n+2} & \cdots & c_{n+m,n+m} \end{pmatrix} \quad (2.6)$$

$$= \begin{pmatrix} A_1 & A_2 \\ A_3 & A_4 \end{pmatrix},$$

where

$$A_1 = \begin{pmatrix} c_{11} & 0 & \cdots & 0 \\ c_{21} & c_{22} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ c_{n1} & c_{n2} & \cdots & c_{nn} \end{pmatrix} = \begin{pmatrix} \frac{1}{\frac{n\delta+d}{n\delta}} & 0 & \cdots & 0 \\ \frac{1}{(n\delta+d)^2} & \frac{1}{n\delta+d} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ \frac{(n\delta)^{n-1}}{(n\delta+d)^n} & \frac{(n\delta)^{n-2}}{(n\delta+d)^{n-1}} & \cdots & \frac{1}{n\delta+d} \end{pmatrix}, \quad (2.7)$$

$$A_2 = \begin{pmatrix} 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 \end{pmatrix}, \quad (2.8)$$

$$A_3 = \begin{pmatrix} c_{n+1,1} & c_{n+1,2} & \cdots & c_{n+1,n} \\ c_{n+2,1} & c_{n+2,2} & \cdots & c_{n+2,n} \\ \vdots & \vdots & \vdots & \vdots \\ c_{n+m,1} & c_{n+m,2} & \cdots & c_{n+m,n} \end{pmatrix} \\ = \begin{pmatrix} \frac{(n\delta)^n}{(m\gamma+\mu+d)(n\delta+d)^n} & \frac{(n\delta)^{n-1}}{(m\gamma+\mu+d)(n\delta+d)^{n-1}} & \cdots & \frac{n\delta}{(m\gamma+\mu+d)(n\delta+d)} \\ \frac{(n\delta)^n(m\gamma)}{(m\gamma+\mu+d)^2(n\delta+d)^n} & \frac{(n\delta)^{n-1}(m\gamma)}{(m\gamma+\mu+d)^2(n\delta+d)^{n-1}} & \cdots & \frac{(n\delta)(m\gamma)}{(m\gamma+\mu+d)^2(n\delta+d)} \\ \vdots & \vdots & \vdots & \vdots \\ \frac{(n\delta)^n(m\gamma)^{m-1}}{\mathcal{A}(n\delta+d)^n(k+\mu+d)} & \frac{(n\delta)^{n-1}(m\gamma)^{m-1}}{\mathcal{A}(n\delta+d)^{n-1}(k+\mu+d)} & \cdots & \frac{(n\delta)(m\gamma)^{m-1}}{\mathcal{A}(n\delta+d)(k+\mu+d)} \end{pmatrix}, \quad (2.9)$$

$$A_4 = \begin{pmatrix} c_{n+1,n+1} & 0 & \cdots & 0 \\ c_{n+2,n+1} & c_{n+2,n+2} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ c_{n+m,n+1} & c_{n+m,n+2} & \cdots & c_{n+m,n+m} \end{pmatrix} \\ = \begin{pmatrix} \frac{1}{\frac{m\gamma+\mu+d}{m\gamma}} & 0 & \cdots & 0 \\ \frac{1}{(m\gamma+\mu+d)^2} & \frac{1}{m\gamma+\mu+d} & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ \frac{(m\gamma)^{m-1}}{\mathcal{A}(k+\mu+d)} & \frac{(m\gamma)^{m-2}}{(m\gamma+\mu+d)^{m-2}(k+\mu+d)} & \cdots & \frac{1}{k+\mu+d} \end{pmatrix}, \quad (2.10)$$

where \mathcal{A} equals $(m\gamma+\mu+d)^{m-1}$.

FV^{-1} is the next-generation matrix for model (1.3). It then follows that the spectral radius of matrix FV^{-1} is

$$\begin{aligned} \rho(FV^{-1}) &= \frac{(\lambda_1 \Lambda / d)(n\delta)^n}{(m\gamma + \mu + d)(n\delta + d)^n} + \frac{(\lambda_2 \Lambda / d)(n\delta)^n(m\gamma)}{(m\gamma + \mu + d)^2(n\delta + d)^n} \\ &+ \cdots + \frac{(\lambda_m \Lambda / d)(n\delta)^n(m\gamma)^{m-1}}{(m\gamma + \mu + d)^{m-1}(n\delta + d)^n(k + \mu + d)}. \end{aligned} \quad (2.11)$$

According to Theorem 2 in [19], the basic reproduction number of model (1.3) is

$$\begin{aligned} R_0 &= \frac{(\lambda_1 \Lambda / d)(n\delta)^n}{(m\gamma + \mu + d)(n\delta + d)^n} + \frac{(\lambda_2 \Lambda / d)(n\delta)^n(m\gamma)}{(m\gamma + \mu + d)^2(n\delta + d)^n} \\ &+ \cdots + \frac{(\lambda_m \Lambda / d)(n\delta)^n(m\gamma)^{m-1}}{(m\gamma + \mu + d)^{m-1}(n\delta + d)^n(k + \mu + d)}. \end{aligned} \quad (2.12)$$

Therefore, R_0 gives the number of secondary infectious cases produced by an infectious individual during his or her effective infectious period when introduced in a population of susceptible. If $R_0 > 1$, then P_0 becomes unstable and the disease becomes endemic. Moreover, a unique endemic equilibrium $P^* = (S^*, L_1^*, L_2^*, \dots, L_n^*, I_1^*, I_2^*, \dots, I_m^*)$ exists in the interior of Γ . Next, we prove the uniqueness of the endemic equilibrium when $R_0 > 1$.

3. Equilibria

An equilibrium $(S, L_1, L_2, \dots, L_n, I_1, I_2, \dots, I_m)$ of (1.3) satisfies

$$\begin{aligned} 0 &= \Lambda - \lambda S - dS, \\ 0 &= \lambda S - (n\delta + d)L_1, \\ 0 &= n\delta L_{i-1} - (n\delta + d)L_i, \quad i = 2, 3, \dots, n, \\ 0 &= n\delta L_n - (m\gamma + \mu + d)I_1, \\ 0 &= m\gamma I_{j-1} - (m\gamma + \mu + d)I_j, \quad j = 2, 3, \dots, m-1, \\ 0 &= m\gamma I_{m-1} - (k + \mu + d)I_m, \end{aligned} \quad (3.1)$$

where λ is given in Section 1. The disease-free equilibrium $P_0 = (\Lambda/d, 0, 0, \dots, 0, 0, 0, \dots, 0)$ exists for all positive parameter values. Next we consider the existence of endemic equilibria $P^* = (S^*, L_1^*, L_2^*, \dots, L_n^*, I_1^*, I_2^*, \dots, I_m^*)$, $S^* > 0$, $L_i^* > 0$, $I_j^* > 0$, $i = 1, \dots, n$, $j = 1, \dots, m$. First, we introduce the definition and properties of M-matrices. Most of the texts on matrix theory can find them [20].

Definition 3.1. $B_{n \times n}$ is a M-matrix if

- (1) Off-diagonal entries of B are nonpositive, and
- (2) B is positively stable, namely, all eigenvalues of B have positive real parts.

Proposition 3.2. *Properties of M-matrices*

- (1) $B = \alpha I - P$, $P \geq 0$, $\alpha > \rho(P)$, the spectral radius of P .
- (2) B is nonsingular and $B^{-1} \geq 0$.
- (3) There exists $\beta > 0$ such that $B^{-1}x \geq \beta x$ for $x \geq 0$.

According to the above, we know that

$$V = \begin{pmatrix} n\delta + d & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ -n\delta & n\delta + d & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & n\delta + d & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & -n\delta & m\gamma + \mu + d & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & -m\gamma & m\gamma + \mu + d & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & k + \mu + d \end{pmatrix}. \quad (3.2)$$

Proposition 3.3. *The following holds for the matrix V defined above.*

- (1) V is a M-matrix.
- (2) V^{-1} exists and is a nonnegative matrix.
- (3) There exists $\nu > 0$ such that $V^{-1}x \geq \nu x$ for $x \geq 0$.

By Proposition 3.3, we know that

$$\nu = (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} \begin{pmatrix} 1 \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} > 0. \quad (3.3)$$

Then, we obtain the result.

Theorem 3.4. *If $R_0 \leq 1$, then P_0 is the only equilibrium in Γ . If $R_0 > 1$, then a unique endemic equilibrium P^* exists in the interior of Γ .*

Proof. The last $n + m$ equations of (3.1) can be written in the form

$$V \begin{pmatrix} L_1 \\ L_2 \\ \vdots \\ L_n \\ I_1 \\ I_2 \\ \vdots \\ I_m \end{pmatrix} = \begin{pmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}, \quad (3.4)$$

or

$$\begin{pmatrix} L_1 \\ L_2 \\ \vdots \\ L_n \\ I_1 \\ I_2 \\ \vdots \\ I_m \end{pmatrix} = V^{-1} \begin{pmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}. \quad (3.5)$$

Multiplying the row vector $(0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m)$ to (3.5), we have

$$\sum_{j=1}^m \lambda_j I_j = (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) \begin{pmatrix} L_1 \\ L_2 \\ \vdots \\ L_n \\ I_1 \\ I_2 \\ \vdots \\ I_m \end{pmatrix} = (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} \begin{pmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}. \quad (3.6)$$

Using $\lambda = \sum_{j=1}^m \lambda_j I_j$, we obtain

$$\begin{aligned} \sum_{j=1}^m \lambda_j I_j &= (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} \begin{pmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} \\ &= (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} \begin{pmatrix} S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} \sum_{j=1}^m \lambda_j I_j. \end{aligned} \quad (3.7)$$

Because $\sum_{j=1}^m \lambda_j I_j \neq 0$, then

$$1 = (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} \begin{pmatrix} S \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} = (0, 0, \dots, 0, \lambda_1, \lambda_2, \dots, \lambda_m) V^{-1} S \begin{pmatrix} 1 \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} = \nu S. \quad (3.8)$$

It is clear that the equation $\nu S = 1$ has a unique positive solution $S^* = 1/\nu$ in the interval $(0, \Lambda/d)$ when $R_0 > 1$. Substitute $S^* = 1/\nu$ into (3.1), and we obtain $L_1^*, \dots, L_n^*, I_1^*, \dots, I_n^*$ are unique positive solution. So the endemic equilibrium P^* is unique when $R_0 > 1$. \square

4. Stability of the Equilibria

In this section, we employ the direct Lyapunov method with a Lyapunov function of the form

$$\sum A_i (X_i(t) - X_i^* \ln X(t)), \quad (4.1)$$

where A_i is a properly selected constant, X_i is the population of the i th compartment, and X_i^* is the equilibrium level, to study properties of this model. This function is referenced in

many papers [21–23], including the models with multiple parallel infectious stages [4, 24] and models with nonlinear incidence rates of different forms [25–28].

Now we are ready to proceed to the global properties of the model.

Theorem 4.1. *If $R_0 \leq 1$, the disease-free equilibrium $P_0 = (\Lambda/d, 0, 0, \dots, 0, 0, 0, \dots, 0)$ is globally asymptotically stable in Γ .*

Proof. Consider the function

$$W = \sum_{i=1}^n A_i L_i + \sum_{j=1}^m B_j I_j, \quad (4.2)$$

where A_i and B_j ($i = 1, 2, \dots, n-1$; $j = 1, 2, \dots, m-2$) are properly selected constants. Their values are as follows:

$$\begin{aligned} A_1 &= (n\delta)^n (m\gamma)^{m-1} > 0, \\ A_2 &= (n\delta)^{n-1} (n\delta + d) (m\gamma)^{m-1} > 0, \\ A_3 &= (n\delta)^{n-2} (n\delta + d)^2 (m\gamma)^{m-1} > 0, \\ &\vdots \\ A_n &= (n\delta) (n\delta + d)^{n-1} (m\gamma)^{m-1} > 0, \\ B_1 &= (n\delta + d)^n (m\gamma)^{m-1} > 0, \\ B_2 &= - \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_1 S) - (n\delta + d)^n (m\gamma)^{m-2} (m\gamma + \mu + d) \right], \\ B_3 &= - \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_2 S) + (n\delta)^n (m\gamma)^{m-3} (m\gamma + \mu + d) (\lambda_1 S) \right. \\ &\quad \left. - (n\delta + d)^n (m\gamma)^{m-3} (m\gamma + \mu + d)^2 \right], \\ &\vdots \\ B_{m-1} &= - \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_{m-2} S) + (n\delta)^n (m\gamma)^{m-3} (m\gamma + \mu + d) (\lambda_{m-3} S) \right. \\ &\quad \left. + \dots + (n\delta)^n (m\gamma) (m\gamma + \mu + d)^{m-3} (\lambda_1 S) - (n\delta + d)^n (m\gamma) (m\gamma + \mu + d)^{m-2} \right], \\ B_m &= - \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_{m-1} S) + (n\delta)^n (m\gamma)^{m-3} (m\gamma + \mu + d) (\lambda_{m-2} S) \right. \\ &\quad \left. + \dots + (n\delta)^n (m\gamma + \mu + d)^{m-2} (\lambda_1 S) - (n\delta + d)^n (m\gamma + \mu + d)^{m-1} \right]. \end{aligned} \quad (4.3)$$

Because $R_0 \leq 1$, the each part of R_0 should be less than 1, that is, $(\lambda_1 \Lambda / d) (n\delta)^n < (m\gamma + \mu + d) (n\delta + d)^n$, $(\lambda_2 \Lambda / d) (n\delta)^n (m\gamma) < (m\gamma + \mu + d)^2 (n\delta + d)^n$, \dots , $(\lambda_m \Lambda / d) (n\delta)^n (m\gamma)^{m-1} <$

$(m\gamma + \mu + d)^{m-1}(n\delta + d)^n(k + \mu + d)$. Therefore, we can obtain that B_2, B_3, \dots, B_m are greater than 0. This function is defined and continuous for all $L_i, I_j > 0$.

Its derivative along the solutions to the system (1.3) is

$$\begin{aligned}
 \dot{W} &= A_1 \dot{L}_1 + \dots + A_n \dot{L}_n + B_1 \dot{I}_1 + \dots + B_m \dot{I}_m = \left[(n\delta)^n (m\gamma)^{m-1} \right] \left[\sum_{j=1}^m \lambda_j I_j S - (n\delta + d) L_1 \right] \\
 &+ \left[(n\delta)^{n-1} (n\delta + d) (m\gamma)^{m-1} \right] [n\delta L_1 - (n\delta + d) L_2] \\
 &+ \dots + \left[(n\delta) (n\delta + d)^{n-1} (m\gamma)^{m-1} \right] [n\delta L_{n-1} - (n\delta + d) L_n] \\
 &+ \left[(n\delta + d)^n (m\gamma)^{m-1} \right] [(n\delta + d) L_n - (m\gamma + \mu + d) I_1] - \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_1 S) \right. \\
 &\quad \left. - (n\delta + d)^n (m\gamma)^{m-2} (m\gamma + \mu + d) \right] [m\gamma I_1 - (m\gamma + \mu + d) I_2] - \dots \\
 &- \left[(n\delta)^n (m\gamma)^{m-2} (\lambda_{m-1} S) + (n\delta)^n (m\gamma)^{m-3} (m\gamma + \mu + d) (\lambda_{m-2} S) + \dots \right. \\
 &\quad \left. + (n\delta)^n (m\gamma + \mu + d)^{m-2} (\lambda_1 S) - (n\delta + d)^n (m\gamma + \mu + d)^{m-1} \right] [m\gamma I_{m-1} - (k + \mu + d) I_m] \\
 &= I_m \left[(n\delta)^n (m\gamma)^{m-1} (\lambda_m S) + (n\delta)^n (m\gamma)^{m-2} (k + \mu + d) (\lambda_{m-1} S) \right. \\
 &\quad \left. + \dots + (n\delta)^n (m\gamma + \mu + d)^{m-2} (k + \mu + d) (\lambda_1 S) - (n\delta + d)^n (m\gamma + \mu + d)^{m-1} (k + \mu + d) \right] \\
 &= I_m (n\delta + d)^n (m\gamma + \mu + d)^m (R_0 - 1).
 \end{aligned} \tag{4.4}$$

If $R_0 \leq 1$, then $\dot{W} \leq 0$. Note that, $\dot{W} = 0$ only if $I_m = 0$. The maximum invariant set in $G = \{(S, L_1, \dots, L_n, I_1, \dots, I_m) : \dot{W} = 0\}$ is the singleton P_0 . The global stability of P_0 when $R_0 \leq 1$ follows from LaSalle's invariance principle [29]. The global attractivity of P_0 and the Lyapunov function W imply that P_0 is also locally stable, since otherwise P_0 will have a homoclinic orbit that is entirely contained in G , contradicting that the largest compact invariant set in G is P_0 . This establishes the global stability of P_0 when $R_0 \leq 1$. \square

Theorem 4.2. *If $R_0 > 1$, the endemic equilibrium $P^* = (S^*, L_1^*, L_2^*, \dots, L_n^*, I_1^*, \dots, I_n^*)$ is globally asymptotically stable in Γ .*

Proof. Let us consider the function

$$\begin{aligned}
 V &= C(S - S^* \ln S) + D(L_1 - L_1^* \ln L_1) + \sum_{i=2}^n E_i (L_i - L_i^* \ln L_i) \\
 &+ F(I_1 - I_1^* \ln I_1) + \sum_{j=2}^{m-1} G_j (I_j - I_j^* \ln I_j) + H(I_m - I_m^* \ln I_m),
 \end{aligned} \tag{4.5}$$

where

$$C = D = 1, \quad E_i = \frac{\lambda S^*}{n\delta L_{i-1}^*}, \quad F = \frac{\lambda S^*}{n\delta L_n^*}, \quad G_j = \frac{\lambda S^*}{m\gamma I_{j-1}^*}, \quad H = \frac{\lambda S^*}{m\gamma I_{m-1}^*}. \quad (4.6)$$

This function is defined and continuous for all $S, L_i, I_j > 0$. By compute the derivative of V along the solutions to the system (1.3), it follows that

$$\begin{aligned} \dot{V} = & (\Lambda - \lambda S - dS) \left(1 - \frac{S^*}{S}\right) + [\lambda S - (n\delta + d)L_1] \left(1 - \frac{L_1^*}{L_1}\right) \\ & + \sum_{i=2}^n \frac{\lambda S^*}{n\delta L_{i-1}^*} [n\delta L_{i-1} - (n\delta + d)L_i] \left(1 - \frac{L_i^*}{L_i}\right) \\ & + \frac{\lambda S^*}{n\delta L_n^*} [n\delta L_n - (m\gamma + \mu + d)I_1] \left(1 - \frac{I_1^*}{I_1}\right) \\ & + \sum_{j=2}^{m-1} \frac{\lambda S^*}{m\gamma I_{j-1}^*} [m\gamma I_{j-1} - (m\gamma + \mu + d)I_j] \left(1 - \frac{I_j^*}{I_j}\right) \\ & + \frac{\lambda S^*}{m\gamma I_{m-1}^*} [m\gamma I_{m-1} - (k + \mu + d)I_m] \left(1 - \frac{I_m^*}{I_m}\right). \end{aligned} \quad (4.7)$$

Recalling that $\Lambda = \lambda S^* + dS^*$, $n\delta + d = \lambda S^*/L_1^* = n\delta L_{i-1}^*/L_i^*$, $m\gamma + \mu + d = n\delta L_n^*/I_1^* = m\gamma I_{j-1}^*/I_j^*$, and that $k + \mu + d = m\gamma I_{m-1}^*/I_m^*$, we obtain

$$\begin{aligned} \dot{V} = & 3\lambda S^* + 2dS^* - dS - \frac{\lambda S^{*2}}{S} - \frac{dS^{*2}}{S} - \frac{L_1\lambda S^*}{L_1^*} - \frac{L_1^*\lambda S}{L_1} \\ & + \sum_{i=2}^n \left(\frac{L_{i-1}\lambda S^*}{L_{i-1}^*} - \frac{L_i\lambda S^*}{L_i^*} - \frac{L_{i-1}L_i^*\lambda S^*}{L_{i-1}^*L_i} + \lambda S^* \right) \\ & + \frac{L_n\lambda S^*}{L_n^*} - \frac{I_1\lambda S^*}{I_1^*} - \frac{L_nI_1^*\lambda S^*}{L_n^*I_1} + \lambda S^* \\ & + \sum_{j=2}^{m-1} \left(\frac{I_{j-1}\lambda S^*}{I_{j-1}^*} - \frac{I_j\lambda S^*}{I_j^*} - \frac{I_{j-1}I_j^*\lambda S^*}{I_{j-1}^*I_j} + \lambda S^* \right) \\ & + \frac{I_{m-1}\lambda S^*}{I_{m-1}^*} - \frac{I_m\lambda S^*}{I_m^*} - \frac{I_{m-1}I_m^*\lambda S^*}{I_{m-1}^*I_m} + \lambda S^* \\ = & dS^* \left(2 - \frac{S^*}{S} - \frac{S}{S^*} \right) + \lambda S^* \left(n + m + 2 - \frac{S^*}{S} - \frac{L_1^*S}{L_1S^*} - \frac{L_2^*L_1}{L_2L_1^*} - \dots \right. \\ & \left. - \frac{L_n^*L_{n-1}}{L_nL_{n-1}^*} - \frac{I_1^*L_n}{I_1L_n^*} - \frac{I_1I_2^*}{I_2I_1^*} - \dots - \frac{I_{m-1}I_m^*}{I_mI_{m-1}^*} - \frac{I_m}{I_m^*} \right). \end{aligned} \quad (4.8)$$

Applying the inequality

$$\frac{a_1 + a_2 + \dots + a_n}{n} \geq \sqrt[n]{a_1 a_2 \dots a_n}, \quad \text{for } a_i \geq 0, \quad i = 1, \dots, n, \quad (4.9)$$

we have

$$\dot{V} \leq 0. \quad (4.10)$$

Therefore, $dV/dt < 0$ for all $S, L_i, I_i > 0$, provided that S^*, L_i^*, I_i^* are positive, where the equality $dV/dt = 0$ holds only on the straight line $S = S^*, L_i/L_i^* = I_i/I_i^*$. It is easy to see that for both these systems, P^* is the only equilibrium state on this line. Therefore, by Lyapunov-LaSalle asymptotic stability theorem [30, 31], the positive equilibrium state P^* is globally asymptotically stable in Γ . \square

5. Conclusion

According to the different length of the latent period and the infectious period of TB, in this paper, we proposed a general n -stage SP model with bilinear incidence to study the transmission dynamics of TB. What to do to make the results more accurate and tally with the actual situation. We prove that the global dynamics are completely determined by the basic reproduction number R_0 . If $R_0 \leq 1$, then the disease-free equilibrium P_0 is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, the unique endemic equilibrium P^* is globally asymptotically stable in the interior of the feasible region, and the disease persists at the endemic equilibrium.

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