Mathematical Model of Tuberculosis Spread within Two Groups of Infected Population

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Abstract

In this paper, we study an SVEIR disease model of tuberculosis transmission dynamics in which the infected population is divided into two groups, namely infectious infected and noninfectious infected population. The equilibrium points and the basic reproduction number $R_0$ are determined. The stability analysis of the model was conducted by considering the basic reproduction number $R_0$. We show that if $R_0 < 1$, then the disease-free equilibrium is locally asymptotically stable. If $R_0 > 1$, then a unique endemic equilibrium is locally asymptotically stable.

Mathematics Subject Classification: 92D30, 93A30, 93C10, 93D20

Keywords: basic reproduction number, stability, SVEIR, tuberculosis
1 Introduction

Tuberculosis is an infectious disease caused by a *Mycobacterium tuberculosis*. This bacterium is a bacillus bacterium which is acid resistant so that someone who has been infected by this bacterium requires a long time to get recovered. Tuberculosis can spread and infect others via active tuberculosis coughs, sneezes, or spreading granules. Those are malnourished, weak immune system, or continuously breathing air contaminated with tuberculosis bacterium highly vulnerable to the disease. Tuberculosis is a deadly disease. In 2014, there were 9.6 million cases reported; in which 58% of them appeared in South-East Asia and Western Pasific regions. However, globally, the incidents were found to be the largest in India, Indonesia, and China, who contributed 23%, 10%, and 10% respectively to the global incidents of the disease [3].

Many researchers have developed a mathematical model and analysis regarding the transmission of tuberculosis. For instance, F. Nyabadza and M. Kgosimore [5] formulated a compartmental model for tuberculosis with two age classes, children and adults. E. Rohaeti, S. Wardatun, and A. Andriyati [7] described the phenomenon of the spreading of tuberculosis in Bogor West Java Indonesia into a mathematical model used SIR model. In this paper, we modify and analyze a tuberculosis spread model with two groups of infected population that was introduced by Blower et al. [1] and has been developed by Ozcaglar et al. [6]. Modifications are done by considering the assumption that exposed individual can move naturally into recovered population and it is assumed that individual who has been recovered can not be re-infected by tuberculosis. Modifications of the model are also done by adding $V$ compartment [4], namely vaccinated population, so that this model is called SVEIR model.

The organization of this paper is as follows. In the next section, modification of tuberculosis spread model with two groups of infected population is formulated. In Section 3, the basic reproduction number and the existence of equilibria are investigated. The local stability of the disease-free and endemic equilibria are proved in Section 4. In the last section, we give some conclusions.

2 The Model Formulation

In this section, we introduce the modification of tuberculosis spread model with two groups of infected population. The total population is divided into six compartments: the susceptible population ($S$), the vaccinated population ($V$), the exposed population ($E$), the infectious infected population ($I_I$), the noninfectious infected population ($I_N$), and the recovered population ($R$).

It is assumed that the rate of incoming individuals into susceptible population is constant $\gamma$. New infections result from contacts between a susceptible and an infectious infected individual with an incidence rate $\beta S(t)I_I(t)$. Susceptible
individual can move into exposed population with fraction \((1 - p)\), \(0 < p < 1\), moves into infectious infected population with fraction \(pf\), \(0 < f < 1\), or moves into noninfectious infected population with fraction \(p(1 - f)\). Susceptible individual can also move into vaccinated population with rate \(\theta\). New infections also result from contacts between a vaccinated and an infectious infected individual with an incidence rate \(\beta V(t)I_I(t)\). In this case, the transmission rate, \(\beta\), is multiplied by a scaling factor \((1 - \sigma)\), where \(0 < \sigma < 1\) is the efficacy of the vaccine. Exposed individual can move into infected population with rate \(v\). A fraction \(q\), \(0 < q < 1\), of exposed population progresses to infectious infected population, and the remaining \((1 - q)\) fraction progresses to noninfectious infected population. Exposed and infected individual can recover naturally and move into recovered population with rate \(c\). The natural mortality rate for the six compartments is \(\mu\) and the mortality rate due to tuberculosis for infectious and noninfectious infected population is \(\mu_T\). The dynamical transfer among the six compartments is depicted in the following transfer diagram.

![Figure 1: The transfer diagram of tuberculosis transmission](image)

Based on our assumptions and the transfer diagram, the model can be described by six ordinary differential equations as follow:

\[
\begin{align*}
\frac{dS}{dt} &= \gamma - \beta SI_I - (\mu + \theta)S, \\
\frac{dV}{dt} &= \theta S - \mu V - (1 - \sigma)\beta VI_I, \\
\frac{dE}{dt} &= (1 - p)\beta SI_I + (1 - \sigma)\beta VI_I - (\mu \nu + c)E, \\
\frac{dI_I}{dt} &= pf\beta SI_I + qvE - (\mu + \mu_T + c)I_I, \\
\frac{dI_N}{dt} &= p(1 - f)\beta SI_I + (1 - q)vE - (\mu + \mu_T + c)I_N, \\
\frac{dR}{dt} &= c(E + I_I + I_N) - \mu R, \\
\end{align*}
\]
with \( N(t) = S(t) + V(t) + E(t) + I_I(t) + I_N(t) + R(t) \) is the total population at time \( t \). The initial value for the system (1) is \( S(0) = S_0 \geq 0, V(0) = V_0 \geq 0, E(0) = E_0 \geq 0, I_I(0) = I_0 \geq 0, I_N(0) = I_{N0} \geq 0, R(0) = R_0 \geq 0, \) and \( N(0) = N_0 \geq 0. \) All parameters are assumed to be positive. The feasible region from the system (1) is described by Lemma 2.1.

**Lemma 2.1.** The set \( \Omega = \{(S, V, E, I_I, I_N, R) \in \mathbb{R}_{+}^6 : 0 \leq N \leq \frac{\gamma}{\mu + \theta} + N_0, 0 \leq S \leq \frac{\gamma}{\mu + \theta} + S_0 \} \) is a feasible region that is nonnegative and bounded from the system (1).

**Proof.** From the system (1), the dynamics of the total population \( N(t) \) is given by:

\[
\frac{dN}{dt} = \gamma - \mu N - \mu_T (I_I + I_N) \leq \gamma - \mu N. \quad (2)
\]

Solving the inequality (2) yields

\[
0 \leq N \leq \frac{\gamma}{\mu} + N_0. \quad (3)
\]

Next, from the first equation of the system (1), we have

\[
\frac{dS}{dt} = \gamma - \beta SI_I - (\mu + \theta)S \leq \gamma - (\mu + \theta)S. \quad (4)
\]

Solving the inequality (4) yields

\[
0 \leq S \leq \frac{\gamma}{\mu + \theta} + S_0. \quad (5)
\]

From the inequality (3) and (5), we have the feasible region that is nonnegative and bounded from the system (1).

### 3 The Basic Reproduction Number

System (1) has the disease-free equilibrium \( T_0 = \left( \frac{\gamma}{\mu + \theta}, \frac{\theta \gamma}{\mu (\mu + \theta)}, 0, 0, 0, 0 \right) \) and the endemic equilibrium \( T^* = (S^*, V^*, E^*, I_I^*, I_N^*, R^*) \), where

\[
S^* = \frac{\gamma}{\beta I_I^* + \mu + \theta}, \quad V^* = \frac{\theta S^*}{\mu + (1 - \sigma) \beta I_I^*},
\]
\[
E^* = \frac{(1 - p) \beta S^* I_I^* + (1 - \sigma) \beta V^* I_I^*}{\mu + v + c}, \quad I_I^* = \frac{q V^*}{\mu + \mu_T + c - pf \beta S^*},
\]
\[
I_N^* = \frac{p(1 - f) \beta S^* I_I^* + (1 - q) v E^*}{\mu + \mu_T + c}, \quad R^* = \frac{c (E^* + I_I^* + I_N^*)}{\mu}.
\]
From the system (1), the matrices of $F$ and $V$ at the disease-free equilibrium $T_0$ are

$$ F = \begin{pmatrix} 0 & \frac{(1-p)\beta \gamma}{\theta+\mu} + \frac{(1-\sigma)\beta \theta \gamma}{\mu(\theta+\mu)} & 0 \\ 0 & \frac{pf \beta \gamma}{\theta+\mu} & 0 \\ 0 & \frac{p(1-f)\beta \gamma}{\theta+\mu} & 0 \end{pmatrix} $$

and

$$ V = \begin{pmatrix} \mu + v + c & 0 & 0 \\ -qv & \mu + \mu_T + c & 0 \\ -(1-q)v & 0 & \mu + \mu_T + c \end{pmatrix}. $$

The basic reproduction number, denoted by $R_0$, is thus given by [9],

$$ R_0 = \rho(FV^{-1}) = \frac{pf \beta \gamma \mu(\mu + v + c) + qv((1-p)\beta \gamma + (1-\sigma)\beta \theta \gamma)}{\mu(\mu + v + c)(\theta + \mu)(\mu + \mu_T + c)}. $$

In the following, the existence of equilibria will be discussed in Theorem 3.1.

**Theorem 3.1.** For the system (1), there is always the disease-free equilibrium $T_0$. Moreover, the endemic equilibrium $T^*$ is unique and positive if and only if $R_0 > 1$.

**Proof.** From equation (6), we have

$$ I^*_1(A_1I^*_1^2 + A_2I^*_1 + A_3) = 0, \tag{7} $$

where

$$ A_1 = (\mu + \mu_T + c)(\mu + v + c)(1-\sigma)\beta^2 > 0, $$

$$ A_2 = (\mu + \mu_T + c)(\mu + v + c)\beta \mu + (qv(1-\sigma)^2 \beta^2 \theta \gamma)/\mu $$

$$ + (\mu + \mu_T + c)(\theta + \mu)(\mu + v + c)(1-\sigma)\beta(1-R_0), $$

$$ A_3 = \mu(\mu + v + c)(\theta + \mu)(\mu + \mu_T + c)(1-R_0). $$

One of the three roots of the equation (7) is $I^*_1 = 0$ which results $S^* = \frac{\gamma}{\mu+\delta}, V^* = \frac{\theta \gamma}{\mu(\mu+\theta)}, E^* = 0, I_N^* = 0$, and $R^* = 0$. This solution is $T_0$ and this achieves the proof that there is always the disease-free equilibrium $T_0$.

Two other roots ($I^*_2$ and $I^*_3$) of the equation (7) is the completion of

$$ A_1I^*_2^2 + A_2I^*_2 + A_3 = 0. \tag{8} $$

From equation (8), two conditions that must be satisfied are

$$ I^*_2 + I^*_3 = -\frac{A_2}{A_1}, $$

$$ I^*_2I^*_3 = \frac{A_3}{A_1}. \tag{9} $$
Suppose $R_0 > 1$, then $A_3 < 0$. Based on condition (9), we have $I_{t2}^* I_{t3}^* < 0$ which is only satisfied if $I_{t2}^*$ and $I_{t3}^*$ have opposite signs. So there is only one positive root $I_1^*$ so that $S^*, V^*, E^*, I^*_N, R^*$ unique with positive values by equation (6). This proves that if $R_0 > 1$, then $T^*$ is unique and positive.

Suppose the endemic equilibrium $T^*$ is unique and positive. We will prove that $R_0 > 1$. Suppose $R_0 < 1$, then $A_2 > 0$ and $A_3 > 0$. Based on condition (9), we have $I_{t2}^* + I_{t3}^* < 0$ and $I_{t2}^* I_{t3}^* > 0$ which are only satisfied if $I_{t2}^* < 0$ and $I_{t3}^* < 0$. So there is no positive endemic equilibrium $T^*$. Contradiction.

Suppose $R_0 = 1$, then $A_2 > 0$ and $A_3 = 0$. Based on conditions (9), we have $I_{t2}^* + I_{t3}^* < 0$ and $I_{t2}^* I_{t3}^* = 0$ which are only satisfied if one root is zero and the other root is negative. So there is no positive endemic equilibrium $T^*$. Contradiction. Consequently, the assumption is wrong. This proves that if the endemic equilibrium $T^*$ is unique and positive, then $R_0 > 1$.

4 Local Stability of Equilibria

In this section, we show that $T_0$ is locally asymptotically stable if $R_0 < 1$ and $T^*$ is locally asymptotically stable if $R_0 > 1$.

**Theorem 4.1.** The disease-free equilibrium $T_0$ is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

**Proof.** Linearizing system (1) gives the Jacobian matrix at $T_0$ as follows:

$$J_{T_0} = \begin{pmatrix}
    J_{11} & 0 & 0 & J_{14} & 0 & 0 \\
    J_{21} & J_{22} & 0 & J_{24} & 0 & 0 \\
    0 & 0 & J_{33} & J_{34} & 0 & 0 \\
    0 & 0 & J_{43} & J_{44} & 0 & 0 \\
    0 & 0 & J_{53} & J_{54} & J_{55} & 0 \\
    0 & 0 & J_{63} & J_{64} & J_{65} & J_{66}
\end{pmatrix}, \quad (10)$$

where

$$J_{11} = -(\theta + \mu), \quad J_{44} = \frac{p f \beta \gamma}{\theta + \mu} - (\mu + \mu_T + c),$$

$$J_{14} = -\frac{\beta \gamma}{\theta + \mu}, \quad J_{53} = (1 - q)v,$$

$$J_{21} = \theta, \quad J_{54} = \frac{p(1 - f) \beta \gamma}{\theta + \mu},$$

$$J_{22} = -\mu, \quad J_{55} = -(\mu + \mu_T + c),$$

$$J_{24} = -\frac{(1 - \sigma) \beta \theta \gamma}{\mu(\theta + \mu)}, \quad J_{63} = c,$$

$$J_{43} = \frac{p f \beta \gamma}{\theta + \mu},$$

$$J_{45} = -\frac{p f \beta \gamma}{\theta + \mu},$$

$$J_{56} = -\frac{p f \beta \gamma}{\theta + \mu}.$$
\begin{align*}
J_{33} &= -(\mu + v + c), \\
J_{34} &= \frac{(1 - p)\beta\mu\gamma + (1 - \sigma)\beta\theta\gamma}{\mu(\theta + \mu)}, \\
J_{43} &= qv, \\
J_{64} &= c, \\
J_{65} &= c, \\
J_{66} &= -\mu.
\end{align*}

The characteristic equation \(|J_{T_0} - \lambda I| = 0\) of (10) is

\begin{equation}
(\lambda - J_{11})(\lambda - J_{22})(\lambda - J_{55})(\lambda - J_{66})(\lambda^2 + a_1\lambda + a_2) = 0, \tag{11}
\end{equation}

where

\begin{align*}
a_1 &= (\mu + v + c) + (\mu + \mu_T + c) - \frac{pf\beta\gamma}{\theta + \mu}, \\
a_2 &= (\mu + v + c)(\mu + \mu_T + c)(1 - R_0).
\end{align*}

From the equation (11), we have four negative eigenvalues as follow:

\begin{align*}
\lambda_1 &= J_{11} = -(\theta + \mu), & \lambda_3 &= J_{55} = -(\mu + \mu_T + c), \\
\lambda_2 &= J_{22} = -\mu, & \lambda_4 &= J_{66} = -\mu,
\end{align*}

while \(\lambda_5\) and \(\lambda_6\) can be obtained by solving the quadratic equation below:

\begin{equation}
\lambda^2 + a_1\lambda + a_2 = 0. \tag{12}
\end{equation}

Suppose \(R_0 < 1\), then

\begin{equation}
\frac{pf\beta\gamma}{\theta + \mu} < (\mu + \mu_T + c). \tag{13}
\end{equation}

The inequality (13) and \(R_0 < 1\) lead \(a_1 > 0\) and \(a_2 > 0\).

From equation (12), two conditions that must be satisfied are

\begin{align*}
\lambda_5 + \lambda_6 &= -a_1 < 0, \\
\lambda_5\lambda_6 &= a_2 > 0. \tag{14}
\end{align*}

The value of \(\lambda_5\) and \(\lambda_6\) which satisfies the condition (14) is \(\lambda_5 < 0\) and \(\lambda_6 < 0\).

Suppose \(R_0 > 1\), then \(a_2 < 0\). Based on condition (14), we have \(\lambda_5\lambda_6 < 0\) which is only satisfied if \(\lambda_5\) and \(\lambda_6\) have opposite signs.

According to [8], \(T_0\) is stable if and only if all eigenvalues of \(J_{T_0}\) are negative and \(T_0\) is unstable if and only if there is at least one positive eigenvalue of \(J_{T_0}\). So this achieves the proof that the disease-free equilibrium \(T_0\) is locally asymptotically stable if \(R_0 < 1\) and unstable if \(R_0 > 1\).
Theorem 4.2. The endemic equilibrium $T^*$ is locally asymptotically stable if $R_0 > 1$.

Proof. Suppose

$$
\varphi = pf\beta\gamma\mu(\mu + v + c) + qv\beta\gamma((1-p)\mu + (1-\sigma)\theta) \\
- \mu(\mu + v + c)(\theta + \mu)(\mu + \mu_T + c).
$$

If $R_0 = 1$, then $\varphi = 0$ and the disease-free equilibrium $T_0$ has zero eigenvalue and all other eigenvalues have negative real parts. The zero eigenvalue has a right eigenvector $(u_1, u_2, u_3, u_4, u_5, u_6)$ and a left eigenvector $(v_1, v_2, v_3, v_4, v_5, v_6)$ as follows:

- $u_1 < 0$,
- $u_2 = \frac{\theta((1-\sigma)(\theta + \mu) + \mu)}{\mu^2}u_1 < 0$,
- $u_3 = -\frac{(\theta + \mu)((1-p)\mu + (1-\sigma)\theta)}{\mu(\mu + v + c)}u_1 > 0$,
- $u_4 = -\frac{(\theta + \mu)^2}{\beta\gamma}u_1 > 0$,
- $u_5 = -\frac{v(1-q)(\theta + \mu)((1-p)\mu + (1-\sigma)\theta)}{\mu(\mu + v + c)(\mu + \mu_T + c)} + \frac{p(1-f)(\theta + \mu)}{(\mu + \mu_T + c)}u_1 > 0$,
- $u_6 = -\frac{c(\theta + \mu)((1-p)\mu + (1-\sigma)\theta)((\mu + \mu_T + c) + (1-q)v)}{\mu^2(\mu + v + c)(\mu + \mu_T + c)}u_1$
  \[ \quad - \frac{c(\theta + \mu)((\theta + \mu)(\mu + \mu_T + c) + p(1-f)\beta\gamma)}{\beta\gamma\mu(\mu + \mu_T + c)}u_1 > 0, \]

- $v_1 = 0$,
- $v_2 = 0$,
- $v_3 > 0$,
- $v_4 = \frac{(\mu + v + c)}{qv}v_3 > 0$,
- $v_5 = 0$,
- $v_6 = 0$.

According to [2], we have

$$
a = \sum_{k,i,j=1}^{6} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(T_0, 0),
$$

$$
b = \sum_{k,i=1}^{6} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \varphi}(T_0, 0).
$$

(15)
The partial derivatives from the system (1) is
\[
\frac{\partial^2 f_3}{\partial x_3 \partial \varphi}(T_0, 0) = \frac{1}{\mu(\theta + \mu)(\mu + \mu T + c)}, \quad \frac{\partial^2 f_3}{\partial x_1 \partial x_4}(T_0, 0) = (1 - p)\beta,
\]
\[
\frac{\partial^2 f_3}{\partial x_4 \partial \varphi}(T_0, 0) = \frac{2}{qv\mu(\theta + \mu)}, \quad \frac{\partial^2 f_3}{\partial x_2 \partial x_4}(T_0, 0) = (1 - \sigma)\beta,
\]
\[
\frac{\partial^2 f_4}{\partial x_3 \partial \varphi}(T_0, 0) = \frac{1}{\beta\gamma((1 - p)\mu + (1 - \sigma)\theta)}, \quad \frac{\partial^2 f_4}{\partial x_1 \partial x_4}(T_0, 0) = pf\beta,
\]
\[
\frac{\partial^2 f_4}{\partial x_4 \partial \varphi}(T_0, 0) = \frac{2}{\mu(\theta + \mu)(\mu + v + c)}.
\]

Equation (15) gives
\[
\begin{align*}
    a &= 2v_3 u_1 u_4 \frac{\partial^2 f_3(T_0, 0)}{\partial x_1 \partial x_4} + 2v_3 u_2 u_4 \frac{\partial^2 f_3(T_0, 0)}{\partial x_2 \partial x_4} + 2v_4 u_1 u_4 \frac{\partial^2 f_4(T_0, 0)}{\partial x_1 \partial x_4} \\
    &= 2v_3 u_1 u_4 (1 - p)\beta + 2v_3 u_2 u_4 (1 - \sigma)\beta + 2v_4 u_1 u_4 pf\beta < 0
\end{align*}
\]

and
\[
\begin{align*}
    b &= v_3 u_3 \frac{\partial^2 f_3(T_0, 0)}{\partial x_3 \partial \varphi} + v_3 u_4 \frac{\partial^2 f_3(T_0, 0)}{\partial x_4 \partial \varphi} + v_4 u_3 \frac{\partial^2 f_4(T_0, 0)}{\partial x_3 \partial \varphi} + v_4 u_4 \frac{\partial^2 f_4(T_0, 0)}{\partial x_4 \partial \varphi} \\
    &= \frac{v_3 u_3}{\mu(\theta + \mu)(\mu + \mu T + c)} + \frac{2v_3 u_4}{qv\mu(\theta + \mu)} + \frac{v_4 u_3}{\beta\gamma((1 - p)\mu + (1 - \sigma)\theta)} \\
    &\quad + \frac{2v_4 u_4}{\mu(\theta + \mu)(\mu + v + c)} > 0.
\end{align*}
\]

The value of \(a\) and \(b\) satisfies condition (iv) in [2]. When \(\varphi\) changes from negative (\(R_0 < 1\)) to positive (\(R_0 > 1\)), then the disease-free equilibrium \(T_0\) changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium \(T^*\) becomes positive and locally asymptotically stable. So this achieves the proof that the endemic equilibrium \(T^*\) is locally asymptotically stable if \(R_0 > 1\).

### 5 Conclusions

In this paper, we propose an SVEIR model of tuberculosis within two groups of infected population. The local dynamics of the model was completely determined by considering the basic reproduction number \(R_0\). We proved that if \(R_0 < 1\), then the disease-free equilibrium \(T_0\) is asymptotically stable. If \(R_0 > 1\), then \(T_0\) becomes unstable and a unique endemic equilibrium \(T^*\) exists and asymptotically stable.
References


Received: April 14, 2016; Published: July 2, 2016