Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2024, 2024:91
https://doi.org/10.28919/cmbn/8716
ISSN: 2052-2541

DYNAMICAL ANALYSIS OF TUBERCULOSIS DISEASE WITH SVEIR MODEL

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Abstract. In this article, we propose a tuberculosis model with drug-sensitive (DS-TB) and multidrug-resistant (MDR-TB). The population is divided into 6 sub-population, namely susceptible (S), vaccinated (V), latent (E), active DS-TB (I_s), active MDR-TB (I_r), and recovered (R). There are two equilibrium points, i.e. disease-free equilibrium (DFE) point and endemic equilibrium (EE) point. The basic reproduction number $(\mathscr{R}_0)$ is determined by using the next generation matrix method. It can be shown that the DFE point is locally and globally asymptotically stable when $\mathscr{R}_0 < 1$. Meanwhile, the EE point is exist if $\mathscr{R}_0 > 1$ and locally asymptotically stable when it holds Routh-Hurwitz criterion. The numerical simulation is conducted to illustrate the analysis results.

Keywords: tuberculosis; multidrug-resistant; basic reproduction number; stability analysis; Routh-Hurwitz criterion.

2020 AMS Subject Classification: 37N25, 92D30.

1. INTRODUCTION

Tuberculosis is an infectious disease caused by the Mycobacterium tuberculosis and can affect the lungs or other parts of the body. This disease is transmitted through the droplets of infected individuals [1]. Tuberculosis has become a major global health issue and is currently

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Received June 18, 2024

one of the top 10 causes of death. Despite significant advancements in the treatment and control of TB, it has been revealed by WHO statistical reports that globally, one-third of the human population is exposed to TB [2].

Tuberculosis has two stages of infection. The first stage of TB infection is called the latent stage. During this period, an individual does not show any symptoms of infection and cannot transmit the disease to others. Whereas, in the second stage called active TB infection, individuals with active TB may show symptoms and can infect susceptible individuals. The WHO global strategy for the prevention, treatment and control of tuberculosis in 2015–2035, known as the End TB Strategy, calls for an early diagnosis of TB targeting an 80% incidence reduction and death from tuberculosis by 90% by 2030. TB prevention may involve BCG vaccination, screening of high-risk individuals, early detection, and case treatment. In most tuberculosis-endemic countries, BCG vaccination is recommended for tuberculosis prevention efforts and is usually given soon after birth [3].

Based on the drug responses, tuberculosis can be categorized by sensitive and resistant. Drug-sensitive TB (DS-TB) means that infectious people can be treated with the usual medicine. Meanwhile drug-resistant is infectious people who become resistant to the drugs used to treat TB. This means that the drug is no more effective to kill the tuberculosis bacteria. The patient becomes resistant also when TB drugs are used inappropriately, such as the patient stops treatment prematurely. Multidrug-resistant TB (MDR-TB) is resistant to at least 2 most effective first-line TB drugs, isoniazid and rifampin. Thus, MDR-TB patients need more complicated treatment than the DS-TB patient and take longer to recover [1].

The mathematical model approach is one of the useful tools and can be used to study the dynamic behavior of a disease. There are several epidemic model that study about tuberculosis transmission. One of simple epidemic model is the SIR model consisting of the susceptible, infected, and recovered class considered by Ali et al. [4]. It is well known that TB disease also has a latent phase. Here are some TB studies with exposed classes, which is when a disease in the body is still unable to transmit and does not show symptoms [5, 6, 7, 8]. Baba et al. [5] presented the susceptible, exposed, and infected (SEI) model with slow and fast progression of infection. The models in [8] assumes that individual who have recovered have

chances to be re-infected again by contact of TB patients while in [6] assumes that individual who have recovered have immunity so they can not to be re-infected. Furthermore, some of these models were developed into more complex model in order to be more inline with their reality. For example, in [9, 10, 11] the vaccinated class is considered because the vaccine given to reduce the risk of getting tuberculosis. Based on these studied, it was found that the vaccine plays important roles in disease prevention and disease spread control. Mathematical model by including vaccinated class is also carried out on the spread of influenza and COVID-19 disease that has the similarities in the mode of transmission [12, 13]. Their numerical simulation results verify that increase vaccination rate effectively can reduce the spread of disease. Several studies that involved the drugs response have also been conducted [14, 15, 16]. Xu et al. [14] developed SEIR model with focused on prevention and control of drug resistant (DR-TB). The researchers found that decreasing the probability of transmission and the progression rate in patients with DR-TB, and also increasing treatment and the recovery rate of DR-TB patients, can help achieve the objective of the End TB Strategy. Bhadauria et al. [15] using SIQR model with Quarantine class suggests that TB in India may be eliminated by 2035 if the treatment success rate could be achieved to 95%, contact tracing and also isolating at least 50% of MDR-TB. Mengistu and Witbooi [16] developed a model for the dynamics transmission of MDR-TB with optimal control and cost-effectiveness analysis. The study found that the most effective control factor for eliminating MDR-TB transmission among single strategies is successful treatment for DS-TB whereas with different combined strategies, the combination of social distancing and DS-TB treatment is more effective and cheaper than other combinations.

In this article, we propose a mathematical model by modified [5, 6, 16]. In this research, we present SVEIR model with some assumptions in Section 2. In Section 3, we provide the non-negative and boundness solution. The equilibrium points, basic reproduction number, and the stability of equilibrium points are provided in Section 4 and Section 5. The numerical simulation was carried out in Section 6 and the conclusion was given in Section 7.

2. Model Development

In this study, the population is divided into 6 classes, namely susceptible class (S), vaccinated class (V), latent class(E), active DS-TB class (I_s), active MDR-TB class (I_r), recovered class (R). The model construction in this research uses assumptions as follows.

noitemsep,nolistsep Vaccinations are given to newborn babies, but some babies are not vaccinated because their health conditions make it impossible. Thus, babies who receive the vaccine enter the (V) vaccinated class [16].

noiitemsep,noliistsep Vaccines are not completely effective for life so vaccinated individuals can become susceptible [16].

noiiitemsep,noliiistsep Latent individuals cannot transmit the disease so transmission occurs due to contact with active TB individuals [5].

noivtemsep,nolivstsep Individuals with active TB can return to the latent class if the therapy given is not effective [5].

novtemsep,nolvstsep TB-DS individuals can become MDR-TB if they do not undergo treatment according to the rules [16].

novitemsep,nolvistsep Individuals with active TB can be cured if treatment therapy is carried out completely [6].

noviitemsep,nolviistsep Individuals will become active TB, both DS-TB and MDR-TB after going through the latent phase.

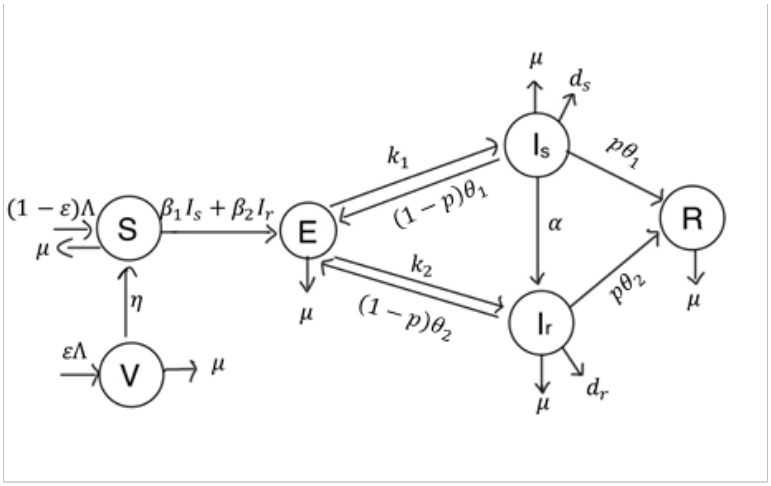


FIGURE 1. Flow diagram of the model

The recruitment rate is divided into 2, namely those entering class S and those entering class V because there are newborns who are vaccinated at a rate of ε. Over time, immunity can weaken so that individuals who have been vaccinated can become susceptible and enter the Susceptible class at a rate of η. The infected individuals can transmit the disease, namely DS-TB (I_s) at a rate of β_1 and MDR-TB (I_r) at a rate β_2. Individuals in the Infected class are given therapy at a rate p and these individuals will return to the latent class because the therapy is ineffective. Active TB individuals who are sensitive to drugs will become resistant at a rate α if they do not adhere to treatment. In the active TB class, the individuals must do treatment until completed so that the individual can enter the recovered class at a rate θ_1 and θ_2. The natural death rate occurs in each classes is assumed to be equal and is given at a rate μ. The death rate of disease for infected individuals is at a rate d_s and d_r.

Based on the diagram in Figure 1, we have the following system of non-linear ordinary differential equations:

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\varepsilon)\Lambda + \eta V - (\beta_1 I_s + \beta_2 I_r) S - \mu S \\
\frac{dV}{dt} &= \varepsilon\Lambda - (\eta + \mu) V \\
\frac{dE}{dt} &= (\beta_1 I_s + \beta_2 I_r) S + (1-p)\,\theta_1 I_s + (1-p)\,\theta_2 I_r - (k_1 + k_2 + \mu) E \\
\frac{dI_s}{dt} &= k_1 E - (\theta_1 + \alpha + \mu + d_s) I_s \\
\frac{dI_r}{dt} &= k_2 E + \alpha I_s - (\theta_2 + + \mu + d_r) I_r \\
\frac{dR}{dt} &= p\theta_1 I_s + p\theta_2 I_r - \mu R
\end{aligned}
\tag{2.1}
$$

3. The Non-Negative and Boundedness of Solution

In this section, we prove the non-negative and boundness solution of model (2.1).

Theorem 3.1. *All solution of the model (2.1) subject to non-negative initial values are non-negative and ultimately bounded.*

Proof. First, we show the non-negative solution of V with a non-negative initial value. Let $V < 0$ for some $t > 0$. We can find $t_* > 0$ such that

$$V(t_*^-) \geq 0, V(t_*) = 0, V(t_*^+) < 0$$

Based on the system (1), we obtain

$$\left.\frac{dV}{dt}\right|_{t=t_*} = \varepsilon\Lambda > 0$$

This means that $V(t) > 0$ on $(t_*, t_* + \varepsilon)$ for arbitrary small positive constant ε. Hence, this leads to a contradiction, which concludes that V is non-negative for all $t \geq 0$. As a result, $V(t) \geq 0$ for all $t \geq 0$. By using the similar way, we can show that the other variables are non-negative. So, all the solutions are positive for all $t \geq 0$.

Total population defined as the number of living humans in the population. So, the total population $N(t)$ can be obtained by adding up all sub-populations in system (2.1), $N(t) = S(t) + V(t) + E(t) + I_s(t) + I_r(t) + R(t)$. By substituting the derivatives in system (2.1) and simplifying, we obtain

$$\begin{aligned}\frac{dN}{dt} &= \Lambda - \mu S - \mu V - \mu E - \mu I_s - \mu I_r - \mu R - d_s I_s - d_r I_r \\ &= \Lambda - \mu N - d_s I_s - d_r I_r \\ &\leq \Lambda - \mu N\end{aligned}$$

Upon integration we get

$$N(t) \leq N_0 e^{-\mu t} + \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right),$$

where $N(0)$ is the initial value. It is clear that

$$\lim_{t\to\infty} \leq 0,$$

thus $N(t)$ is bounded with $N(t) \leq \frac{\Lambda}{\mu}$. Hence, we can see that the feasible closed region of model (2.1) is

$$\Omega = \left\{(S, V, E, I_s, I_r, R) \in \mathbb{R}_+^6 : N = S + V + E + I_s + I_r + R \leq \frac{\Lambda}{\mu}\right\}$$

□

4. Equilibrium Points and Basic Reproduction Number

For dynamical analysis, the last equation of model (2.1) can be reduced because other equations do not involve variable R. Hence, we consider only first five equations. Let $X = (S,V,E,I_s,I_r)$, the equilibrium point can be obtained by setting $\frac{dX}{dt} = \vec{0}$. We get $V = \frac{\varepsilon\Lambda}{\eta+\mu}, S = \frac{\Lambda(\eta+\mu-\eta\mu)}{(\eta+\mu)(\beta_1 I_s+\beta_2 I_r+\mu)}, E = \frac{(\theta_1+\alpha+\mu+d_s)(\theta_2+\mu+d_r)}{(\theta_1+\alpha+\mu+d_s)k_2+k_1\alpha} I_r, I_s = \frac{k1(\theta_2+\mu+d_r)}{(\theta_1+\alpha+\mu+d_s)k_2+k_1\alpha} I_r$. By substituting $I_r = 0$, we have a disease-free equilibrium point (Q_1)

$$Q_1 = (S_1,V_1,E_1,I_{s1},I_{r1}) = \left(\frac{\Lambda A_5}{A_4\mu}, \frac{\varepsilon\Lambda}{A_4}, 0, 0, 0\right) .$$

Next, if we substituting $I_r \neq 0$ with suppose that $A_1 = \theta_1+\alpha+\mu+d_s; A_2 = \theta_2+\mu+d_r; A_3 = A_1k_2+k_1\alpha; A_4 = \eta+\mu; A_5 = \eta+\mu-\eta\mu; A_6 = \beta_1k_1A_2+\beta_2A_3; A_7 = \theta_1k_1A_2+\theta_2A_3; A_8 = k_1+k_2+\mu; A_9 = A_1A_2A_8-(1-p)A_7$ then we obtain the endemic equilibrium points,

$$\begin{aligned}
S_2 &= \frac{A_9}{A_6} \\
V_2 &= \frac{\varepsilon\Lambda}{A_4} \\
E_2 &= \frac{A_1A_2(\Lambda A_5A_6 - A_4A_9\mu)}{A_4A_6A_9} \\
I_{s2} &= \frac{k_1A_2(\Lambda A_5A_6 - A_4A_9\mu)}{A_4A_6A_9} \\
I_{r2} &= \frac{A_3(\Lambda A_5A_6 - A_4A_9\mu)}{A_4A_6A_9}
\end{aligned}$$

Next, the basic reproduction number $(\mathscr{R}_0)$ is defined as the number of secondary infections produced by one infective. The basic reproduction number can be determined by the next generation matrix method. This method involved a compartment causes infection, that is $Z = E, I_s, I_r$. So, we have

$$\frac{dZ}{dt} = \mathscr{F}(Z) - \mathscr{V}(Z)$$

where

$$\mathscr{F}(Z) = \begin{pmatrix} (\beta_1 I_s+\beta_2 I_r)S \\ 0 \\ 0 \end{pmatrix}; \qquad \mathscr{V}(Z) = \begin{pmatrix} -(1-p)\,\theta_1 I_s - (1-p)\,\theta_2 I_r + (k_1+k_2+\mu)E \\ -k_1E + (\theta_1+\alpha+\mu+d_s)I_s \\ -k_2E - \alpha I_s + (\theta_2+\mu+d_r)I_r \end{pmatrix}$$

the Jacobian matrix of $\mathscr{F}$ and $\mathscr{V}$ evaluated at disease-free equilibrium point (Q_1) are respectively given by F and V as follows

$$F = \frac{\partial \mathscr{F}_i(x_1)}{\partial x_j} = \begin{pmatrix} 0 & \beta_1 S & \beta_2 S \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} = \begin{pmatrix} 0 & \frac{\beta_1 \Lambda A_5}{A_4 \mu} & \frac{\beta_2 \Lambda A_5}{A_4 \mu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

$$V = \frac{\partial \mathscr{V}_i(x_1)}{\partial x_j} = \begin{pmatrix} k_1 + k_2 + \mu & -(1-p)\theta_1 & -(1-p)\theta_2 \\ -k_1 & \theta_1 + \alpha + \mu + d_s & 0 \\ -k_2 & -\alpha & \theta_2 + \mu + d_r \end{pmatrix}$$

$$= \begin{pmatrix} A_8 & -(1-p)\theta_1 & -(1-p)\theta_2 \\ -k_1 & A_1 & 0 \\ -k_2 & -\alpha & A_2 \end{pmatrix}$$

The basic reproduction number $(\mathscr{R}_0)$ which is defined as the spectral radius of the next generation method, and denoted by $\rho(FV^{-1})$ is evaluated to:

$$\mathscr{R}_0 = \rho(FV^{-1}) = \frac{A_5 A_6 \Lambda}{A_4 A_9 \mu}$$

Thus, E_2, I_{s2} and I_{r2} can be expressed as

$$E_2 = \frac{A_1 A_2 \mu}{A_6}(\mathscr{R}_0 - 1)$$
$$I_{r2} = \frac{A_3 \mu}{A_6}(\mathscr{R}_0 - 1)$$
$$I_{s2} = \frac{k_1 A_2 \mu}{A_6}(\mathscr{R}_0 - 1)$$

Because the parameter values are all positive so that A_1, A_2, A_3, and A_6 are also positive. Thus, E_2, I_{s2} and I_{r2} exist if $\mathscr{R}_0 > 1$.

Theorem 4.1. *The model* (2.1) *has two equilibrium points as follows:*

(1) The disease-free equilibrium point $Q_1 = (S_1, V_1, E_1, I_{s1}, I_{r1}) = \left(\frac{\Lambda A_5}{A_4 \mu}, \frac{\varepsilon \Lambda}{A_4}, 0, 0, 0\right)$

(2) The endemic equilibrium point $Q_2(S_2, V_2, E_2, I_{s2}, I_{r2})$

5. THE STABILITY ANALYSIS OF EQUILIBRIUM POINTS

Theorem 5.1. *The disease-free equilibrium point* Q_1 *of model (2.1) is locally asymtotically stable in domain* Ω *if* $\mathscr{R}_0 < 1, a_0 > 0, a_1 > 0, a_3 > 0$, *and* $a_1 a_2 - a_3 a_0 > 0$.

Proof. The Jacobian matrix evaluated at Q_1 is given by

$$J(Q_1) = \begin{pmatrix} -\mu & \eta & 0 & -\frac{\beta_1 \Lambda A_5}{A_4 \mu} & -\frac{\beta_2 \Lambda A_5}{A_4 \mu} \\ 0 & -A_4 & 0 & 0 & 0 \\ 0 & 0 & -A_8 & \frac{\beta_1 \Lambda A_5}{A_4 \mu} + (1-p)\theta_1 & \frac{\beta_2 \Lambda A_5}{A_4 \mu} + (1-p)\theta_2 \\ 0 & 0 & k_1 & -A_1 & 0 \\ 0 & 0 & k_2 & \alpha & -A_2 \end{pmatrix}$$

The first two eigenvalues are $\lambda_1 = -\mu < 0, \lambda_2 = -A_4 < 0$, while the other three eigenvalues in the form of polynomial as follow,

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

where:

$a_1 = A_1 + A_2 + A_8$

$a_2 = A_1A_2 + A_2A_8 + A_1A_8 - k_2\left(\frac{\beta_2 \Lambda A_5}{A_4 \mu} + (1-p)\theta_2\right) - k_1\left(\frac{\beta_1 \Lambda A_5}{A_4 \mu} + (1-p)\theta_1\right)$

$a_3 = A_9(1 - \mathscr{R}_0)$

By Routh-Hurwitz criterion, the equilibrium point Q_1 is locally asymptotic stable if and only if hold conditions:

- $a_1 > 0$,
- $a_3 > 0$,
- $a_1a_2 - a_3 > 0$

We can see that a_1 is always positive, $a_3 = A_9(1 - \mathscr{R}_0) > 0$ if $\mathscr{R}_0 < 0$ and other conditions will be proven by numerical simulations. Therefore all solutions of the characteristic polynomial have negative real parts if $\mathscr{R}_0 < 0, a_1 > 0, a_3 > 0$, and $a_1a_2 - a_3 > 0$. So that, the disease-free equilibrium point is locally asymptotically stable. □

The global stability of equilibrium points offers a more comprehensive understanding of the model's dynamics beyond just local stability. Analyzing the global stability of the equilibrium point is crucial for a more precise interpretation because it doesn't rely on the initial size of subpopulations, thus capturing the dynamic essence of the model [17]. In this context, we use the Castillo-Chavez method to examine the global stability of the Disease-Free Equilibrium

(DFE). In this method the system is written as,

$$\frac{dY}{dt} = F(Y,Z)$$
$$\frac{dZ}{dt} = G(Y,Z)$$

where the $Y \in \mathbb{R}^m$ is the class of uninfected individuals and $Z \in mathbbR^n$ is the class of infected individuals. Suppose $Q_1 = (Y^0, \vec{0})$ is the disease-free equilibrium point, Q_1 is globally asymptotic stable if $\mathscr{R}_0 < 1$ and meets the following conditions

(1) for $\frac{dY}{dt} = (Y,0), Y^0$ globally asymptotically stable

(2) $G(Y,Z) = AZ - \hat{G}(Y,Z), \hat{G}(Y,Z) \geq 0, \forall (Y,Z) \in \Omega$

where $A = D_Z G(Y^0,0)$ is the M-matrix (the off diagonal elements of A are non-negative) and Ω is the region.

Theorem 5.2. *The disease-free equilibrium point of the system $Q_1 = (Y^0,0)$ is globally asymptotic stable if $\mathscr{R}_0 < 1$ and following the conditions (H1) and (H2).*

Proof. In order to prove the theorem of Castillo-Chavez method [18], first the model can be rewrite as

$$\frac{dY}{dt} = F(Y,Z) = \begin{pmatrix} (1-\varepsilon)\Lambda + \eta V - (\beta_1 I_s + \beta_2 I_r + \mu)S \\ \varepsilon\Lambda - (\eta + \mu)V \end{pmatrix}$$

$$\frac{dZ}{dt} = G(Y,Z) = \begin{pmatrix} (\beta_1 I_s + \beta_2 I_r)S + (1-p)\theta_1 I_s + (1-p)\theta_2 I_r - (k_1 + k_2 + \mu)E \\ k_1 E - (\theta_1 + \alpha + \mu + d_s)I_s \\ k_2 E + \alpha I_s - (\theta_2 + \mu + d_r)I_r \end{pmatrix}$$

$$G(Y,\vec{0}) = \vec{0}$$

where $Y = (S,V) \in \mathbb{R}^2_+$ and $Z = (E,I_s,I_r) \in \mathbb{R}^3_+$. We consider that,

$$\frac{dY}{dt} = F(Y,\vec{0}) = \begin{pmatrix} (1-\varepsilon)\Lambda + \eta V - \mu S \\ \varepsilon\Lambda - (\eta + \mu)V \end{pmatrix}$$

which we get,

$$Y(t) = \begin{pmatrix} S(t) \\ V(t) \end{pmatrix} = \begin{pmatrix} \frac{(1-\varepsilon)\Lambda}{\mu} + \frac{\varepsilon\Lambda}{\eta+\mu} + S(0)e^{-\mu t} + V(0)e^{-(\eta+\mu)t} \\ \frac{\varepsilon\Lambda}{\eta+\mu} + V(0)e^{-(\eta+\mu)t} \end{pmatrix}$$

It is observed that $S(t) \to \frac{\Lambda(\eta+\mu-\eta\mu)}{\mu(\eta+\mu)}$ and $V(t) \to \frac{\varepsilon\Lambda}{\eta+\mu}$ as $t \to \infty$, showing that Y^0 is globally asymptotically stable and condition (H1) is satisfied. Next, we notice that A is Jacobian matrix evaluated at the disease-free point,

$$A = \begin{pmatrix} -(k_1+k_2+\mu) & \frac{\beta_1\Lambda(\eta+\mu-\eta\mu)}{(\eta+\mu)\mu} + (1-p)\theta_1 & \frac{\beta_2\Lambda(\eta+\mu-\eta\mu)}{(\eta+\mu)\mu} + (1-p)\theta_2 \\ k_1 & -(\theta_1+\alpha+\mu+d_s) & 0 \\ k_2 & \alpha & -(\theta_2+\mu+d_r) \end{pmatrix}$$

$$\dot{G}(Y,Z) = \begin{pmatrix} (\beta_1 I_s + \beta_2 I_r)\left(\frac{\Lambda(\eta+\mu-\eta\mu)}{(\eta+\mu)\mu} - S\right) \\ 0 \\ 0 \end{pmatrix}$$

It is seen that $G(Y,Z)$ are non-negative, and condition (H2) also satisfied. Since both condition are satisfied, the disease-free point Q_1 is globally asymptotically stable in domain Ω. □

Theorem 5.3. *The endemic equilibrium point Q_2 of model (2.1) exist if $\mathscr{R}_0 > 1$ and locally asymtotically stable in domain Ω if $b_1 > 0, b_4 > 0, \Delta_2^* > 0$, and $\Delta_3^* > 0$.*

Proof. The Jacobian matrix evaluated at Q_2 is given by

$$J(Q_2) = \begin{pmatrix} -(\mu(\mathscr{R}_0-1)+\mu) & \eta & 0 & -\frac{\beta_1 A_9}{A_6} & -\frac{\beta_2 A_9}{A_6} \\ 0 & -A_4 & 0 & 0 & 0 \\ \mu(\mathscr{R}_0-1) & 0 & -A_8 & \frac{\beta_1 A_9}{A_6} + (1-p)\theta_1 & \frac{\beta_2 A_9}{A_6} + (1-p)\theta_2 \\ 0 & 0 & k_1 & -A_1 & 0 \\ 0 & 0 & k_2 & \alpha & -A_2 \end{pmatrix}$$

The first eigenvalue is $\lambda_1 = -A_4 < 0$, while the other eigenvalues in the form of polynomial as follow,

$$\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0$$

where:

$b_1 = A_1 + A_2 + A_8 + \mu\mathscr{R}_0$

$b_2 = A_2\mu\mathscr{R}_0 + (A_1+A_8)(A_2+\mu\mathscr{R}_0) + A_1A_8 - k_1\left(\frac{\beta_1 A_9}{A_6} + (1-p)\theta_1\right) - k_2\left(\frac{\beta_2 A_9}{A_6} + (1-p)\theta_2\right)$

$b_3 = \mu\mathscr{R}_0(A_1(A_2+A_8) + A_2A_8 - (1-p)(k_1\theta_1 + k_2\theta_2)) - \frac{A_9}{A_6}\mu(k_1\beta_1 + k_2\beta_2)$

$b_4 = A_9\mu(\mathscr{R}_0 - 1)$

The endemic equilibrium point Q_2 is locally asymptotically stable if only if following Routh-Hurwitz criterion

- $b_1 > 0$,
- $b_4 > 0$,
- $\Delta_2^* = b_1 b_2 - b_3 > 0$,
- $\Delta_3^* = b_3 \Delta_2^* - (b_1)^2 b_4 > 0$

We can see that b_1 is always positive, $b_4 = A_9 \mu(\mathscr{R}_0 - 1) > 0$ if $\mathscr{R}_0 > 0$, and other conditions will be proven by numerical simulations. □

6. NUMERICAL SIMULATION

Numerical simulation aims to illustrate the results of the analysis that has been obtained in the previous section. In this section, a numerical simulation will be shown with initial values $(S,V,E,I_s,I_r) = (50,18,10,7,5)$. By taking values of parameters $\beta_1 = 0.006356, \beta_2 = 0.003458, p = 0.8$ in the first simulation, we have basic reproduction number $\mathscr{R}_0 = 0.311 < 1$ with the disease-free equilibrium point $Q_1 = (61.1143, 1.3856, 0, 0, 0)$. By using this parameters, we hold Routh-Hurwitz criterion, that is $a_1 a_2 - a_3 = 2.179 > 0$. Based on the analytical analysis, the equilibrium point Q_1 is locally asymptotically stable. Thus, by using the initial values above, the graph shown in Figure 2 is obtained.

Next, by using a set of parameter values $\beta_1 = 0.06356, \beta_2 = 0.03458, p = 0.57$, we have $\mathscr{R}_0 = 3.99 > 1$ with the disease-free equilibrium point $Q_1 = (61.1143, 1.3856, 0, 0, 0)$ and the endemic equilibrium point $Q_2 = (15.2812, 1.3856, 11.6773, 0.3111, 0.8159)$. By using this parameters, we have $\lambda^4 + (2.116)\lambda^3 + (1.1705)\lambda^2 + (0.06916)\lambda + 0.0028$. These also holds Routh-Hurwitz criterion $\Delta_2^* = 2.407 > 0$ and $\Delta_3^* = 0.1539 > 0$. From the analytical analysis, the equilibrium point Q_2 is locally asymptotically stable when $\mathscr{R}_0 > 1$ and the graph shown in Figure 3.

Based on Figure 2, the susceptible populations S and the vaccinated populations V progress to their state value while populations E, I_s and I_r towards zero as time goes on. This suggests that if $\mathscr{R}_0 < 1$, then the disease will disappear from a population. From the graph it can be seen that the solution will go to the disease-free equilibrium point Q_1 when the value is $\mathscr{R}_0 < 1$, thus the simulation confirm that from the results of the disease-free equilibrium point analysis

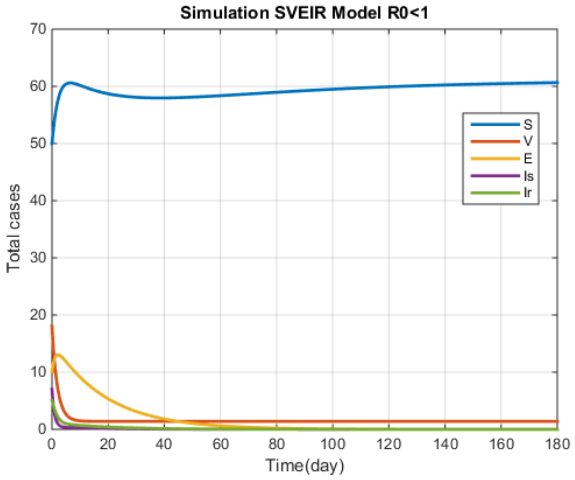


FIGURE 2. Simulation when $\mathscr{R}_0 < 1$

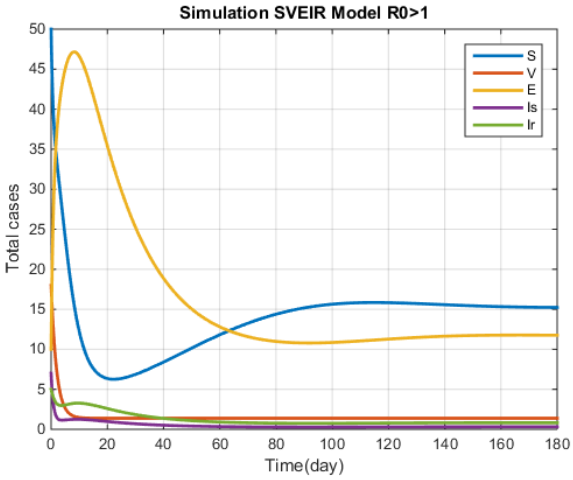
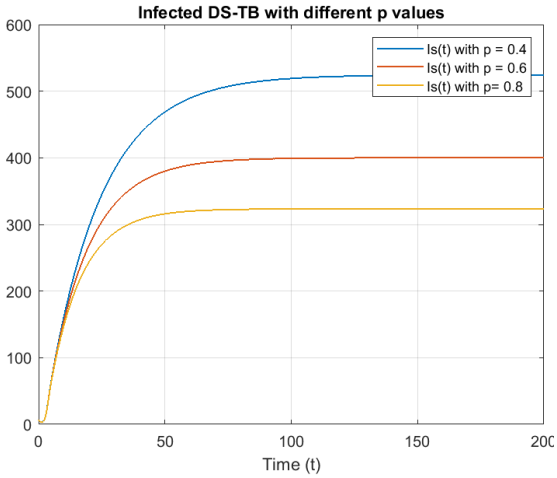
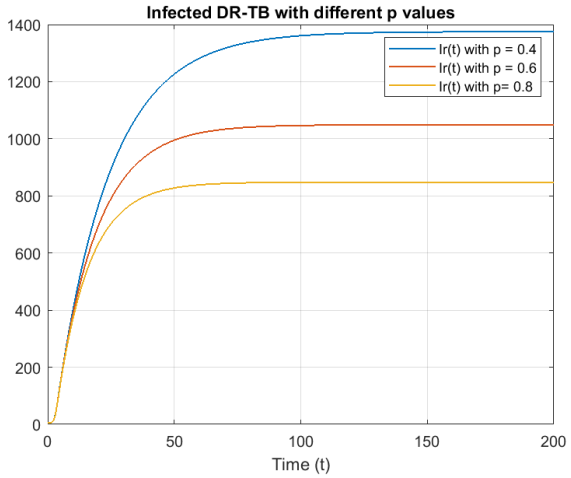


FIGURE 3. Simulation when $\mathscr{R}_0 > 1$

is locally asymptotically stable. Based on Figure 3, for the value of $\mathscr{R}_0 > 1$ the solution of the model both susceptible, vaccinated, latent and infected populations will go to a value that is an endemic equilibrium point as time goes on. This means that if $\mathscr{R}_0 > 1$ then the system will remain endemic and the disease will continue to spread in the population.





(A) The effect of treatment rate on the number of I_s (B) The effect of treatment rate on the number of I_r

FIGURE 4. The number of infected class with different p values

From the basic reproduction number formula and the parameter values, we can reduce the number of $\mathscr{R}_0$ by decreasing the rate of infection β_1 and β_2. In order to decreasing the rate of

infection we can increasing the rate of treatment (p). Figure 4 illustrate the effect of treatment rate on the number of the infected population. It is shows that enhancing both treatment is indispensable for reducing the overall infected TB patient population. This shows that tuberculosis disease can be controlled by treating infective people until the treatment is completed.

7. CONCLUSION

The mathematical model of tuberculosis disease spread is in the form of a nonlinear ordinary differential equation system $SVEIR$. The system has two equilibrium points, namely disease-free equilibrium (DFE) points and endemic equilibrium (EE) points, and has a basic reproduction number ($\mathscr{R}_0$). Based on stability analysis, the disease-free equilibrium point is locally and globally asymptotically stable when $\mathscr{R}_0 < 1$. Furthermore, the endemic equilibrium point exists if $\mathscr{R}_0 > 1$ and locally asymptotic stable if the Routh–Hurwitz criterion is met. Numerical simulations also support the results of the analysis obtained. By using a parameter that $\mathscr{R}_0 < 1$, the graph solution goes to the disease-free equilibrium point and when the parameter gives $\mathscr{R}_0 > 1$ the graph solution goes to the endemic point. Furthermore, from the basic reproduction number formula we can reduce the number of by decreasing the rate of infection. In order to decreasing the rate of infection we can increasing the rate of treatment. This shows that tuberculosis disease can be controlled by treating infective people until completed treatment.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

REFERENCES

[1] WHO, Tuberculosis, (2024). https://www.who.int/news-room/fact-sheets/detail/tuberculosis.

[2] S. Bagcchi, WHO's global tuberculosis report 2022, The Lancet Microbe 4 (2023), e20. https://doi.org/10.1016/S2666-5247(22)00359-7.

[3] CDC, Testing for tuberculosis, (2024). https://www.cdc.gov/tb/topic/testing.

[4] Z.M. Ali, F.H. Abd Aziz, N.A. Azmi, et al. Numerical solution of SIR model with time delay for transmission of tuberculosis disease, in: 2023 IEEE 11th Conference on Systems, Process & Control (ICSPC), IEEE, Malacca, Malaysia, 2023: pp. 90–95. https://doi.org/10.1109/ICSPC59664.2023.10420197.

[5] I.A. Baba, R.A. Abdulkadir, P. Esmaili, Analysis of tuberculosis model with saturated incidence rate and optimal control, Physica A: Stat. Mech. Appl. 540 (2020), 123237. https://doi.org/10.1016/j.physa.2019.123237.

[6] I. Ullah, S. Ahmad, Q. Al-Mdallal, et al. Stability analysis of a dynamical model of tuberculosis with incomplete treatment, Adv. Differ. Equ. 2020 (2020), 499. https://doi.org/10.1186/s13662-020-02950-0.

[7] K. Das, B.S.N. Murthy, Sk.A. Samad, et al. Mathematical transmission analysis of SEIR tuberculosis disease model, Sensors Int. 2 (2021), 100120. https://doi.org/10.1016/j.sintl.2021.100120.

[8] K. Jain, A. Bhattacharjee, Modeling and stability analysis of SEIRS model for understanding the tuberculosis disease dynamics, AIP Conf. Proc. 2649 (2023), 030056. https://doi.org/10.1063/5.0114135.

[9] A.K. Mengistu, P.J. Witbooi, Mathematical analysis of TB model with vaccination and saturated incidence rate, Abstr. Appl. Anal. 2020 (2020), 6669997. https://doi.org/10.1155/2020/6669997.

[10] A. Kelemu Mengistu, P.J. Witbooi, Modeling the effects of vaccination and treatment on tuberculosis transmission dynamics, J. Appl. Math. 2019 (2019), 7463167. https://doi.org/10.1155/2019/7463167.

[11] Y. Li, X. Liu, Y. Yuan, et al. Global analysis of tuberculosis dynamical model and optimal control strategies based on case data in the United States, Appl. Math. Comput. 422 (2022), 126983. https://doi.org/10.1016/j.amc.2022.126983.

[12] H.F. Huo, K.D. Cao, H. Xiang, Modelling the effects of the vaccination on seasonal influenza in Gansu, China, J. Appl. Anal. Comput. 12 (2022), 407–435. https://doi.org/10.11948/20210306.

[13] M. Zevika, A. Triska, N. Nuraini, et al. On the study of covid-19 transmission using deterministic and stochastic models with vaccination treatment and quarantine, Commun. Biomath. Sci. 5 (2022), 1–19. https://doi.org/10.5614/cbms.2022.5.1.1.

[14] A. Xu, Z. Wen, Y. Wang, W. Wang, Prediction of different interventions on the burden of drug-resistant tuberculosis in China: a dynamic modelling study, J. Glob. Antimicrob. Resist. 29 (2022), 323–330. https://doi.org/10.1016/j.jgar.2022.03.018.

[15] A.S. Bhadauria, H.N. Dhungana, V. Verma, et al. Studying the efficacy of isolation as a control strategy and elimination of tuberculosis in India: A mathematical model, Infect. Dis. Model. 8 (2023), 458–470. https://doi.org/10.1016/j.idm.2023.03.005.

[16] A.K. Mengistu, P.J. Witbooi, Cost-effectiveness analysis of the optimal control strategies for multidrug-resistant tuberculosis transmission in Ethiopia, Int. J. Diff. Equ. 2023 (2023), 8822433. https://doi.org/10.1155/2023/8822433.

[17] R.R. Musafir, A. Suryanto, I. Darti, et al. Stability analysis of a fractional-order monkeypox epidemic model with quarantine and hospitalization, J. Biosafe. Biosecur. 6 (2024), 34–50. https://doi.org/10.1016/j.jobb.2024.02.003.

[18] C. Castillo-Chavez, Z. Feng, W. Huang, On the computation of R_0 and its role on global stability, in: C. Castillo-Chavez, S. Blower, P. Van Den Driessche, et al. (Eds.), Mathematical Approaches for Emerging and Reemerging Infectious Diseases: An Introduction, Springer, New York, 2002: pp. 229–250. https://doi.org/10.1007/978-1-4757-3667-0_13.