Mathematical analysis on SEIR-type model of the Tuberculosis disease spread with vaccination and treatment elements

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Abstract. Tuberculosis (TB) is one of the most contagious diseases that cause many deaths. TB disease is caused by Mycobacterium tuberculosis bacteria that commonly affect the lungs and other organs such as lymph nodes, intestines, kidneys, womb, bones and brain. World Health Organization (WHO) stated that in 2015 there are 60% of TB cases found in developing countries including India, Indonesia, China, Nigeria, Pakistan and South Africa. By 2015 the TB death rate is 1.4 million. One way to reduce the spread of TB disease is vaccination and treatment. The treatment given is in the form of several types of drugs that should be taken by infected individuals within a certain period of time. Therefore, it is necessary to do a scientifically acceptable analysis of the spread of TB disease. Mathematical model for analyzing the spread of TB disease have been widely developed. One is SEIR type. In this model the population is divided into four groups, namely S for susceptible individuals, E for exposed individuals, I for infected individuals, R for recovered individuals. This article discusses the model of SEIR type TB disease with vaccination and treatment.

1. Introduction

Tuberculosis (TB) is one of the leading causes of death in developing countries caused by Mycobacterium tuberculosis. These bacteria generally attack the lungs and some can attack the lymph nodes, intestines or gastrointestinal tract, cerebral membranes and so on. Symptoms of Tuberculosis include coughing, chest pain, shortness of breath, loss of appetite, weight loss, fever, chills, and fatigue [1]. World Health Organization (WHO) reported that in 2015 there are 60% of TB cases found in developing countries including India, Indonesia, China, Nigeria, Pakistan and South Africa. Globally, TB treatment achieves a 52% success rate in 2013 [2]. TB transmission comes from people with smear positive TB that spread germs into the air in droplets when sneezing or coughing. People can be infected if the droplet is inhaled into the respiratory tract [3]. TB infection can be divided into two types, namely latently infected and actively infected. Latent-infected people are called latent TB patients. Latent TB patients will not transmit TB bacteria to people susceptible to TB disease. An active infected person is called an active TB patient. Active TB patients can transmit TB disease to people susceptible to TB disease [4]. The way TB prevention has been done in Indonesia is vaccination and treatment. TB treatment is one of the most efficient measures to reduce the further spread of TB bacteria [3].

The spread of TB disease can be modeled mathematically. Several studies on the spread of TB...
disease have been done. Fredlina et al. [1] developed a model of the spread of TB disease by using SIR type model which considered three compartments of populations i.e. susceptible (S), infected (I), and recovered (R). It was then simulated using the 4th order Runge-Kutta method. The results showed that the spread of TB disease could be controlled from epidemic events by decreasing the rate of transmission and increasing the rate of recovery. One way to reduce the rate of transmission is to keep TB-infected individuals from at the susceptible population, whereas to improve the rate of recovery the treatment needs to be maximized [1]. A SEIR type model considering susceptible, exposed, infected, and recovered populations was also introduced by Juan Wang et al. [5] to analyze the TB spread. The research considered infection in latent period and imperfect treatment. The model expanded by grouping infected peoples according to their time of infection 0. The global asymptotic stability of the endemic equilibrium. The numerical simulation was intended to illustrate the results of the model. Analysis of TB spread using SEIR model was carried out by Syahrini et al. [6]. In the study, vaccination was considered which was administrated to the susceptible population. The vaccination rate highly inversely affects the spread of the TB disease; the higher the vaccination rate, the lower the spread of TB epidemic.

Bhunu et al. [7] discussed the model of TB disease that includes infective treatment and chemoprophylaxis. This model assumed that latently infected individuals can transmit active disease as a result of endogenous reactivation, exogenous re-infection and recurrent disease, some were assumed to transmit active disease after infection. The results showed that infective treatment was more effective in the first years of implementation then chemoprophylaxis was performed for better results. Mlay et al. [8] applied the optimal control theory for the tuberculosis model that included vaccination and treatment. This model control mechanism is associated with latently infected chemoprophylaxis by socializing education on TB. The maximum principle of Pontryagin was used to reduce the number of latent and active patients. Numerical simulations were performed using forward and backward method on the fourth order Runge-Kutta. The results showed that the control measure by providing educational socialization was more effective in controlling TB transmission and infection than latently infected chemoprophylaxis. Time delay in recovery process was considered in SIR model of TB diseases spread studied in [9]. The model included vaccinated susceptible group and gave asymptotically stable condition. The result suggested that there is a critical value for the time delay which may lead to bifurcation.

In this study, the spread of TB disease using SEIR type model is considered. Here, the population is divided into four groups namely susceptible, exposed (latent), infected and recovered. In this model vaccinations are given to susceptible individuals and treatment to the infected individuals. Furthermore, the group of infected individuals is divided into two groups, the first group is first-stage infected individuals and the second group is second-stage infected individuals whose disease is more critical than the first group. Both groups are assumed to perform different treatments. Furthermore, the solution of the model will be simulated by using fourth order Runge-Kutta method.

2. The mathematical model

The spread of TB disease is illustrated in Figure 1. The model employs SEIR type scheme counting the presence of vaccination and treatment. In Figure 1, it is defined that N is the total population. The susceptible group is divided into two groups: the unvaccinated susceptible (S_u) and the vaccinated susceptible (S_v). E represents the latent group of individuals which means the individual has contracted the TB bacteria but has not been infected tuberculosis disease yet. I_1 is a group of first-stage infected individuals and I_2 is a group of second-stage infected individuals. I_2 group suffers more critical TB disease than I_1 group hence both infected groups are given different treatments. R is a group of recovered individuals which come from I_1 or I_2. It is assumed that the population is closed. Vaccines are only given to individuals who have never been infected with TB disease. Individuals who are vaccinated and unvaccinated can fall into groups of latent individuals. Any individual in the I_1 group who fails the treatment will be admitted into the second-stage infected group I_2. Individuals who have recovered may return to recurrence and fall within the second-stage infected group I_2. Individuals who have interacted with sick individuals will fall into groups of latent individuals. Therefore, the mathematical model for the spread of TB disease can be written with the following
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formula.

\[
\frac{dS_u}{dt} = (1 - c)\pi N - \beta_u \frac{I_1 + I_2}{N} S_u - \mu S_u
\]
\[
\frac{dS_v}{dt} = c\pi N - \beta_v \frac{I_1 + I_2}{N} S_v - \mu S_v
\]
\[
\frac{dE}{dt} = q\beta_u \frac{I_1 + I_2}{N} S_u + \beta_v \frac{I_1 + I_2}{N} S_v + \delta I_1 + I_2 \left(1 - \frac{R}{N}\right) - \varepsilon E - pE - \mu E
\]
\[
\frac{dI_1}{dt} = (1 - q)\beta_u \frac{I_1 + I_2}{N} S_u + \varepsilon E - \mu I_1 - \mu_T I_1 - v_1 I_1 - \gamma I_1
\]
\[
\frac{dI_2}{dt} = \gamma I_1 + \alpha R - \mu I_2 - \mu_T I_2 - v_2 I_2
\]
\[
\frac{dR}{dt} = v_1 I_1 + v_2 I_2 + pE - \alpha R - \delta \frac{I_1 + I_2}{N} R - \mu R
\]
\[
N = S_u + S_v + E + I_1 + I_2 + R
\]

Figure 1. SEIR type model of TB disease with vaccination and treatment elements.

The parameters’ definitions and values appeared in the model are presented in Table 1.

Table 1. The parameters’ definitions and values used in the model

| Symbols | Definition | Value (per year) | Value interval | References |
|---------|------------|-----------------|----------------|------------|
| \(c\)   | Rate of vaccination | 0.9             | \(0 < c < 1\)  | [6]        |
| \(\pi\) | Birth rate | 0.02695         | \(0 < \pi < 1\) | [6]        |
| \(\beta_u\) | Transmission rate of the unvaccinated susceptible individuals | 0.35            | \(0 < \beta_u < 1\) | [6]        |
| \(\beta_v\) | Transmission rate of the vaccinated susceptible individuals | 0.35            | \(0 < \beta_v < 1\) | [6]        |
| \(q\)   | Infection probability of the  | 0.5             | \(0 < q < 1\)  | [6]        |
| \(\varepsilon\) | Rate of change from latent to infected individuals | 0.0003          | \(0 < \varepsilon < 1\) | [6]        |
In this study, it is assigned that $N = 111324$ people and the initial values are $S_u(0) = 46000$, $S_v(0) = 46000$, $E(0) = 13000$, $I_1(0) = 4374$, $I_2(0) = 1950$, and $R(0) = 0$ in the unit of the number of people.

### 3. Equilibrium state

To determine the equilibrium points, the population in system (1) is set constant over time, i.e. $\frac{dS_u}{dt} = 0$, $\frac{dS_v}{dt} = 0$, $\frac{dE}{dt} = 0$, $\frac{dI_1}{dt} = 0$, and $\frac{dR}{dt} = 0$. By this setting, one equilibrium point is obtained:

$$E_0 = (S_u, S_v, E, I_1, I_2, R) = \left(\frac{(1-c)\pi N}{\mu}, \frac{c\pi N}{\mu}, 0, 0, 0, 0\right).$$

The equilibrium point is called as free-disease equilibrium. The stability of the equilibrium point can be determined by finding the eigenvalues of the Jacobian matrix of the linearized model. By substituting the parameter values, the recovery rates $v_1 = 0.35$ and $v_2 = 0.35$ give eigenvalues $r_1 = -0.0100, r_2 = -0.0100, r_3 = -0.0100, r_4 = -0.2596, r_5 = -0.6136$, and $r_6 = -0.6601$. Meanwhile, the recovery rates $v_1 = 0.9$ and $v_2 = 0.9$ give eigenvalues $r_1 = -0.0100, r_2 = -0.0100, r_3 = -0.2600, r_4 = -0.0100, r_5 = -1.1631$ and $r_6 = -1.2100$. The obtained eigenvalues are all negative real numbers, thus the equilibrium point is asymptotically stable. Reproduction number $R_0$ can be determined by using the next generation matrix (K) of the system (1). It is obtained that for the tree cases of recovery rates $v_1 = v_2 = 0.35, v_1 = v_2 = 0.7$ and $v_1 = v_2 = 0.9$ the values of K are $-7.1511, -4.6732$, and $-3.9008$ respectively. This results that the three values of $R_0$ are less than 1 ($R_0<1$) meaning that the sick individuals will not transmit the disease to other individuals so that there is no spread of disease in the population and the disease free equilibrium point is asymptotically stable.

### 4. Results and discussion

The model is solved numerically using the fourth order Runge Kutta methods. The results of the solution obtained can be observed in the following figure.
Figure 2. Graphs of each population for recovery rates (a) 0.35, (b) 0.7, and (c) 0.9
Figure 3. Graphs of the number of population in (a) first-stage infected group \( (I_1) \), (b) second-stage infected group \( (I_2) \), (c) recovered group \( (R) \).

Figure 2 represents graphs of the entire populations for recovery rates 0.35, 0.7, and 0.9. All three graphs, Figure 2(a), 2(b), and 2(c), have the same initial population number. It can be observed in the figures that, there is a significant difference on the graphs of recovered population \( (R) \); as the recovery
rate increases the number of recovered individual increases. Figure 3(a) exhibits the number of individuals in the first-stage infected group. The number of individuals in this group decreases and approaches zero at different times for every given recovery rate, for the recovery rates 0.35, 0.7, and 0.9, the number of population in the first-stage infected group start to vanish after 15, 10, and 8 years respectively. Figure 3(b) presents the number of individuals in the second-stage infected group. The number of individuals in this group decreases and approaches zero at different times for every given recovery rate, for the recovery rates 0.35, 0.7, and 0.9, the number of population in the second-stage infected group start to vanish after 12, 8, and 6 years respectively. The number of recovered population can be observed in Figure 3(c). It can be remarked that as the recovery rate gets higher, the number of the recovered population will reach its equilibrium point faster.

5. Conclusion
Based on the above results, the SEIR type model of Tuberculosis disease spread with vaccination and treatment elements has an asymptotically stable equilibrium point. The model’s solutions obtained by using numerical method have the same tendency as the ones obtained from analytical methods presented in the previous researches. According to the simulation for some values of treatment/recovery rates, it can be concluded that the higher the recovery rate is the more rapidly the spread of TB disease decreases to eventually disappear.

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