Mathematical Model Susceptible, Infected and Recovered with Therapy of Tuberculosis Transmission

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Abstract. Tuberculosis (TB) is one of infectious disease caused by bacteria Mycobacterium Tuberculosis which most often attacks the bronchi. Tuberculosis spreads from person to person by direct contact or also through the air. TB is very dangerous and can attack anyone and if it is not seriously treated will cause death. But if TB given treatment seriously this TB will recover. One treatment of TB is with long-term therapy. This therapy is very influential for recovery of infected people of TB. This article discusses the dynamics of the spread of tuberculosis with therapy through mathematical modeling, the model of disease spread adopted is the SIR Model. From the results of the research showed that by giving therapy to TB patients had a positive and significant effect, especially on recovering, the greater the value of the therapy parameters, the higher the patient's recovery rate.

1. Introduction
Tuberculosis (TB) is a contagious disease that is very dangerous and can cause death. TB is caused by the bacterium Mycobacterium tuberculosis which is transmitted through the air and can attack anyone regardless of age or gender. Symptoms of TB sufferers include coughing, chest pain, shortness of breath, loss of appetite, weight loss, fever, cold and fatigue.

Tuberculosis disease is the cause of the number three deaths after cardiovascular disease and respiratory diseases in all age groups, and is the number one that causes death among other infectious diseases [1]. Tuberculosis is still a matter of public health and a global challenge in the world. In the year 1993, the World Health Agency (WHO) proclaimed the global emergency of tuberculosis disease because in most countries in the world TB was not healed, especially infectious diseases (BTA positive). In 1995 it is estimated that each year occurred about 9 million people with a new TB with a death of 3 million. In developing countries, TB's death represents 25 percent of all deaths that are actually preventable. It is estimated that 95 percent of Tuberculous sufferers are in developing countries, and 75 percent of Tuberculosis sufferers are productive age groups (15-50 years). Indonesia is the third-most TB contributor in the world after China and India. Based on TB's prevalence survey in 2013-2014 Indonesian TB prevalence rate in Indonesia is 660 per 100,000 inhabitants. Given the many cases and the high deaths from the disease, it is necessary to improve the knowledge and awareness of all the general public and medical... With the emergence of the HIV/AIDS epidemic in the world, it is estimated that TB sufferers are more than death due to pregnancy, childbirth and nifas. It is shown that TB disease is one of the diseases that concern and should be dealt with seriously through prevention and treatment.
Various measures of prevention and countermeasures and the efforts of socialization are conducted, but the results are not as expected. TB suffers still remain high in different regions. This indicates failure to occur from the prevention side. This is due to many obstacles both technically and non-technical. Such constraints include limited funds, infrastructure limitations, lack of data and information.

To solve these constraints, need a research and thinking that can describe the behavior of spreading TB disease. One way to help understand and identify the spread of TB disease is mathematical modeling. Mathematical models are usually used to simplify the complex state of the system. Mathematical modeling can be utilized to illustrate and inform the spread of TB disease by using certain assumptions that the solution can be obtained both analytic and numeric [3]. The mathematical Model that was formed will be conducted analysis to get a representative of the problems studied. Mathematical modeling is also used to inform, predict, understand and develop strategies to control the spread of infectious diseases through the behavioral assessment of each parameter in the system under various conditions. The last few years of mathematical modeling has become an interesting tool for understanding the epidemic of infectious diseases [4].

One model of infectious disease spread is the SIR model (Susceptible – Infected-Recovered). This Model divides the population into three sub-populations, i.e. susceptible individual sub-populations (Susceptible), individual subpopulation infected (Infected) and individual sub-population cured (Recovered). This article adopts SIR model with development in infected individuals through the addition of parameters on the infected sub population of the individual, the parameters are therapeutic parameters. Therapy or treatment is very important in people with TB disease. Generally patients who are late or have no action such as treatment or therapy will result in death. Addition of therapeutic parameters will affect the level of cure. This article also displays simulations associated with parameters and their effect on the level of healing.

Furthermore, models that have been developed conducted mathematical analysis, through analysis of the specified equilibrium point, further determine the number of reproductive ratios and effects of the therapeutic parameters on the number of reproductive ratios and do Numerical simulation. Simulation is done with functional based programming using Matlab Software.

2. SIR Model with Therapy
An epidemic of SIR (Susceptible-Infected-Recovered) is a model of spreading the disease that divides the population into three sub-populations. That is, the vulnerable individual population (S), the infected sub-population (I) and the individual sub-population are cured (R). In the event that a partially vulnerable sub-population will move to the infected sub-population and subsequently move into the recovered sub-population. The following are given system compartment diagram of disease spread Tuberculosis SIR model:

![Figure 1. Mathematical Model flow Diagram Tuberculosis SIR model](image)

Mathematical models of the distribution compartment diagram of TB disease are:

$$\frac{dS}{dt} = \pi - b \frac{I}{N} S - \mu S$$
With:
\[N = S + I + R\]
\[\frac{dS}{dt} = b \frac{I}{N} - (\mu + \mu_t + c + d)S\]
\[\frac{dI}{dt} = (\mu + \mu_t + c + d)I - \mu R\]
\[\frac{dR}{dt} = (c + d)I - \mu R\]

The rate of change of human population which is vulnerable to against the time
The rate of change of human population infected against the time
The rate of change in human populations that heal against time
S = Population vulnerable to Tuberculosis
I = Vulnerable populations and can be transmitted to other individuals
R = Population cured Tuberculosis disease
b = Rate of disease transmission
c = Rate of healing
\(\mu\) = Rate of death due to other factors
\(\mu_t\) = Rate of death because Tuberculosis
\(\pi\) = Rate of population birth
d = therapy

3. Analysis Of the Model
In this model analysis the first step is to determine the equilibrium points/equilibrium. A system is said to be very concerned, if the system no longer changes in certain conditions of time. To determine the equilibrium of the system of equations (1) is by creating the system:
\[\frac{dS}{dt} = 0; \frac{dI}{dt} = 0 \text{ and } \frac{dR}{dt} = 0\]
\[\pi - b \frac{I}{N}S - \mu S = 0\]  
\[b \frac{I}{N}S - (\mu + \mu_t + c + d)I = 0\]  
\[(c + d)I - \mu R = 0\]

The first equilibrium point is the equilibrium point of disease-free, where at this point the non-existing non-population (I = 0), from the equation (3.1) to the disease-Free State (I = 0), the equilibrium point is obtained:
\[\pi - b \frac{I}{N}S - \mu S = 0\]
\[\pi - \mu S = 0\]
\[S = \frac{\pi}{\mu}\]
\[b \frac{I}{N}S - (\mu + \mu_t + c + d)I = 0\]
\[I = 0\]
\[I(\frac{\mu}{N} - (\mu + \mu_t + c + d) = 0\]
\[-\mu R = 0\]
\[R = 0\]

The disease-free equilibrium point is:
The endemic equilibrium point (I≠0) obtained:

\[
E_0 = (S, I, R) = (S, 0, 0) = \left( \frac{\pi}{\mu}, 0, 0 \right)
\]  

(5)

At the point of Equilibrium disease-free (E_0) It is apparent that the vulnerable sub-population is \( \frac{\pi}{\mu} \), while the infected sub-population and subpopulation recover are not present or equal to zero.

Next if I ≠ 0 or I > 0 means there is already an infected sub-population Indicating that the infected sub-population is likely to transmit Tb disease to another individual. Then of the equation (3.3) obtained:

\[
I = \frac{\mu R}{(c+d)}
\]

\[
R^* = \frac{\pi(c+d)(b-\mu-\mu_t-c-d)}{\mu(\mu+\mu_t+c+d)(b-\mu_t)}
\]

(6)

\[
I^* = \frac{\pi(b-\mu_\mu-\mu_t-c-d)}{\mu(b-\mu_t)}
\]

\[
S^* = \frac{\pi(c+d)}{\mu(b-\mu_t)}
\]

Order I > 0 then \( b > +\mu_t + c + d \),

So that the endemic equilibrium point is

\[
E_1 = (S^*, I^*, R^*) = \left( \frac{\pi(\mu+c+d)}{\mu(b-\mu_t)}, \frac{\pi(b-\mu-\mu_t-c-d)}{\mu(\mu_t+c+d)(b-\mu_t)}, \frac{\pi(c+d)(b-\mu-\mu_t-c-d)}{\mu(\mu+\mu_t+c+d)(b-\mu_t)} \right)
\]

(7)

At the endemic equilibrium point (E_1) indicates that the sub-population is vulnerable, sub-populations of uninvectors and sub-populations recovered already exist.

4. The Basic Reproduction Number of SIR Model with Therapy

Basic Reproduction Number is the number that states the average number of secondary infective individuals due to contracting the primary infectious individual that takes place in the susceptible population. In epidemiology, the spread level of an infectious disease is commonly measured by a value called the basic reproduction ratio (R0). To be freed from TB infection, must be made R_{0}(0)<1. In this case, each sufferer can only spread the disease to an average of less than one new sufferer, so that the disease will eventually disappear. Meanwhile, if R_{0}(0)>1 then each sufferer can spread the disease to an average of more than one new sufferer, so that there will be an epidemic [3]. Calculation of basic reproductive numbers (R_0) based on linearization of a system of differential equations that are approached by disease-free equilibrium points. The equation of the infected compartment has been dilinearsed. Basic reproduction numbers (R_0) can be determined using the next generation Matrix method. In this case the concern for determining the number of reproductive ratios is differential equations in the infected variable (I) namely:
\[ \frac{dl}{dt} = b \frac{I}{N} S - (\mu + \mu_t + c + d) l \]

Obtained:
\[ \psi = \left[b \frac{l}{N} S \right] \tan \varphi = [(\mu + \mu_t + c + d)] \]

By linearization:
\[ F = \left[b \frac{S}{N} - \frac{biS}{N^2} \right] \text{dan } V = [\mu + \mu_t + c + d] \]

And \( V^{-1} = \frac{1}{\mu + \mu_t + c + d} \)

from
\[ K = FV^{-1} = R_0 = \left[b \frac{S}{N} - \frac{biS}{N^2} \right] \frac{1}{\mu + \mu_t + c + d} \]

Substitution equations (3.4) \( E_0 = (S, I, R) = \left(\frac{\pi}{\mu}, 0, 0\right) \) on (3.7)

Obtained:
\[ K = FV^{-1} = \frac{b}{\mu + \mu_t + c + d} \]

The number of reproduction ratios \( (R_0) \) of the SIR model with therapy on the spread of TB disease is:

\[ R_0 = \frac{b}{\mu + \mu_t + c + d} \]  (9)

From the equation (9) can be concluded that:
- \( R_0 < 1 \) is obtained if \( b < \mu + \mu_t + c + d \) and vice versa
- \( R_0 > 1 \) is achieved if \( b > \mu + \mu_t + c + d \)

Death due to other factors \((\mu)\) and death due to tuberculosis \((\mu_t)\) cannot be increased. Therefore, it is healing or treatment for people with TB, so the healing rate \((c)\) and therapeutic \((d)\) will increase. In addition, the rate of disease transmission TB \((b)\) should also be lowered, thereby the spread level of TB infection will be reduced so that the disease can be controlled from epidemic state. So it can be said, from this analysis will be known the most influential parameters of all the parameters that exist in the deployment model of the tuberculosis are the parameters \( b, c \) and \( d \).

5. Numerical Analysis Simulation

5.1. The simulation for \( R_0 < 1 \)

Based on the conditions for the \( R_0 < 1 \), the value is given \( \pi = 500, b = 0.00015, c = 0.027, \mu = 0.0009, d = 0; 0.04; 0.08 \) and \( \mu_t = 0.0001 ; S(0) = 400000 ; I(0) = 50000; R(0) = 25000. \) Further simulation is done using Matlab software.
In the condition \( R_0 < 1 \), Figure 2 indicates that the effect of therapy on susceptible subpopulation is not very significant, this is due to this sub population there is no infected individual yet. Figure 3a shows that the therapeutic effect has been seen significant, meaning that sub-population infected with the therapeutic treatment without therapy is clearly apparent that the infected sub-population without therapy \((d = 0)\) indicates the number of sub-populations slow-loading and long-lasting, on the other hand, the infected sub-population that is given therapy clearly indicates that the number of infected populations decreases rapidly and leads to a stable state or can be said to be extinct. Similarly, in Figure 3b, in sub-population recovered the influence of therapy and without therapy also significant.

5.2. The simulation for \( R_0 > 1 \)

The values of the given parameters are:
\[ \Pi = 500, \ b = 0.0097, \ c = 0.00032, \ \mu = 0.0009, \ \mu_i = 0.0001 \text{ dan } d = 0, 0.4, 0.8. \]

With initial value \( S(0) = 400000, \ I(0) = 50000, \ R(0) = 250000. \) Acquired simulation \( R_0 > 1 \) as follows:
In the condition of $R_0 > 1$, also known as conditions where the disease is endemic means that each sufferer can spread the disease to an average of more than one new sufferer. In the 5.4 figure shows that the therapeutic effect of sub-population susceptible is significant, wherein at $d = 0$ or there is no therapeutic sub-populai susceptible decreases as time goes by, conversely when therapeutic ($d = 0.04$ and $d = 0.8$) Sub Susceptible population increases in line with increasing time. Likewise for sub population Inrcted and sub population of Recovered, the effect of therapy with no therapy is seen significant.

6. Conclusion
The effect of treatment in the form of therapy in the sufferer tuberculosis very significant especially at the level of healing, the greater the value given to the therapeutic parameters, the more likely the TB sufferers will heal. It can be proven or shown on the given chart. In the presence of therapeutic causes decreased sub-population infected and significantly increases sub-population recovered.

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