Effect of the Vaccine on the Dynamics of Spread of Tuberculosis SIR Models

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Abstract. Tuberculosis (TB) is an infectious disease that is very dangerous and causes death. The disease is caused by a pathogen that is not inherited and can be cured. However, the treatment of TB disease is time-consuming and costly. Therefore, prevention is more effective than treatment. The government has made efforts to provide vaccines. This study uses the SIR model, considering the effect of vaccines. The purpose of this study is to estimate the basic reproduction number ($R_0$) from the SIR model and to see how the vaccines can reduce the spread of tuberculosis. The basic reproductive number is often used as a threshold parameter to determine the boundary between extinction and endemic. If $R_0 < 1$, the disease will become extinct; if $R_0 > 1$, the disease is endemic.

Keywords: Tuberculosis, mathematical modeling, vaccine, basic reproduction number

1. Introduction

Tuberculosis (TB) is one of the most dangerous infectious diseases, one of the top ten causes of death in the world. Therefore, TB disease is one of the concerns of all countries in the world, especially Asian countries. The World Health Organization (WHO) reported that in 2017, TB disease infected 10 million people in the world [1]. From the results of the WHO report in 2018, Indonesia was in the third position after China and India. From the results of the 2018 WHO report, the number of TB cases in Indonesia is around 845,000 cases [2]. However, if the ratio of the population to the number of TB cases is calculated, Indonesia is in the first place followed by India and China with a successive ratio of 0.003; 0.001, and 0.0006. TB disease is a special concern for all countries in the world, including Indonesia. According to an estimate, nearly 1 million cases are in Indonesia and only 68% are found and treated. The cases found are still low and those that have not been found and have not been treated have great potential to infect other people. The following is a table of WHO estimates of TB cases in Indonesia [2].
Table 1. Estimate mycobacterium Number of Tuberculosis Cases in Indonesia in 2018

|                          | NUMBER (thousands) | RATE (per 100,000 population) |
|--------------------------|--------------------|--------------------------------|
| Total TB incidence       | 845 (770-923)      | 316 (288-345)                  |
| HIV-positive TB incidence| 21 (8.9-38)        | 7.9 (3.3-14)                   |
| MDR/RR-TB incidence      | 24 (17-32)         | 8.8 (6.2-12)                   |
| HIV-negative TB mortality | 93 (87-99)         | 35 (33-37)                     |
| HIV-positive TB mortality | 5.3 (2.1-9.8)      | 2 (0.79-3.7)                   |

Source: WHO, Global Tuberculosis Report 2019

From Table 1, TB sufferers in Indonesia in 2018 were around 770,000 - 923,000 cases (average 845,000). It is estimated that, on average, per 100,000 population there were 288-345 cases (mean 316). This case is considered high for the spread of infectious diseases and needs serious handling by the Indonesian government in particular.

The following graph shows the development of Tuberculosis cases in Indonesia (Source: WHO, Global Tuberculosis Report 2019)

Figure 1. Development of the Spread of Tuberculosis and HIV-Positive Tuberculosis Cases
Source: WHO, Global Tuberculosis Report 2019

TB disease caused by *mycobacterium tuberculosis* is not a hereditary disease, this disease can affect anyone, regardless of age. TB transmission through droplets and very easily transmitted. To break the chain of transmission, all sufferers should be found and treated. disease TB can be avoided by keeping the dwelling place dark, not humid and air ventilation good enough, sunlight can enter the room because *germs tuberculosis* can die from sunlight. Thus infection or germs that enter the body through breathing or skin wounds can be prevented or at least reduced in number. TB disease is preventable and curable. TB disease treatment is time consuming and costly. Therefore, the term prevention is better than cure very precisely for Tuberculosis. One of the efforts made by the government is to provide vaccines.

Vaccines are suspension of germs or viruses that have been weakened and are used to treat or prevent an infectious disease. Vaccination in Indonesia has been regularly started since 1956 [3]. The vaccines used for tuberculosis, namely Bacille Calmette and Guerin (BCG), are very efficient in preventing transmission to infants and children, and are effective against active TB in adults [4]. In 1973, the BCG comprehensive vaccination was part of the immunization program. It is hoped that the administration or injection of this vaccine will reduce susceptible individuals to latenly-infected and actively-infected individuals, reduce latenly-infected individuals to become actively-infected and reduce the spread of TB disease.

Administration of the BCG vaccine (*Bacillus Calmette Guerin*) for newborns cannot last a lifetime. The BCG vaccine is only effective in childhood, but immunity decreases with age. So
that sufferers of tuberculosis remain high every year. Besides that, not all newborns get the vaccine Bacillus Calmette-Guérin. This is due to both technical and non-technical constraints [5]. These obstacles include the limited knowledge of individuals about Tuberculosis. The lack of understanding about how the spread of tuberculosis occurs and limited funds and information [6]. Technically, to break the chain of transmission, is to find, find and treat as many sufferers as possible. Finding sufferers and being cured more quickly also prevents the potential for immunity or resistance to TB drugs. One way to prevent TB disease transmission is to pay attention to the behavior of each parameter that affects the spread of this disease, this can be done through a mathematical modeling approach [7].

Mathematical modeling is useful for describing the state of a complex system into a simple one. Through the analysis of mathematical models also provide information about the behavior of the spread of Tuberculosis. One of the most important things in the analysis of mathematical models, especially in the study of disease spread systems, is in determining the function of the basic reproduction number ($R_0$) which is also called the threshold number. This threshold number will provide information on each parameter studied and its relationship with the spread of disease.

2. Research Method

2.1 SIR Epidemic Model with Vaccine

One of the models still in use today is the SIR (Susceptible, Infected and Recover) model. This model was first developed by Kermack and McKendrick in 1927. The SIR model has the same structure and assumptions as to the SI model. Its extension is that in the SIR model it is possible for the infected population / community member to recover or recover [8]. In this SIR model, the total population of $N$ is divided into three interconnected sub groups, namely the Susceptible subgroup symbolized by $S(t)$, the Infection subgroup symbolized by $I(t)$ and the cured subgroup symbolized by $R(t)$. In this case the susceptible sub-population partially moves to the soup population of the infection and then moves into the cured sub-population. In this study, it is assumed that the population is constant, and every recovered population will not be infected again. The growth rate of the Susceptible ($S$) sub-population increases with the multiplication of the opportunities for individuals who are not vaccinated ($1 - \sigma$) with birth ($\lambda$) and will decrease with the presence of mortality ($\mu$) and susceptible infection. The growth rate of the Infection subpopulation ($I$) increases with the incidence of susceptible infection and decreases with the presence of natural mortality ($\mu$) and the proportion of movement to the subpopulation heals. The growth rate for the sub-population to recover increases in the presence of vaccine individuals recover from infection and decreases with death ($\mu$). The following is a compartment diagram of the spread of Tuberculosis (TB) SIR Model.

![Figure 2. Compartment Diagram of the Spread of Tuberculosis Model SIR with Vaccine](image)

From Figure 2, a mathematical equation for the spread of Tuberculosis is formed, this equation is called a differential equation system with three variables, namely:
\[
\frac{dS}{dt} = (1 - \sigma)\lambda N - b \frac{I}{N} S - \mu S \quad \text{(2.1)}
\]
\[
\frac{dI}{dt} = b \frac{I}{N} S - (\mu + \delta)I \quad \text{(2.2)}
\]
\[
\frac{dR}{dt} = \delta I + \lambda \sigma N - \mu R \quad \text{(2.3)}
\]

With: \( N = S + I + R \) where:

\( \frac{dS}{dt} \) = rate of change in quantity human population susceptible to time

\( \frac{dI}{dt} \) = rate of change in the number of infected humans against time

\( \frac{dR}{dt} \) = rate of change in the number of human populations who recover over time

\( S \) = population susceptible to being infected with Tuberculosis

\( I \) = population that is susceptible and can be transmitted to other individuals

\( R \) = population recovered from tuberculosis

\( b \) = disease transmission rate

\( \sigma \) = vaccine

\( \delta \) = cure rate

\( \mu \) = death rate due to other factors

\( \mu_t \) = death due to tuberculosis

\( \lambda \) = population birth

3. Results and Discussion

From the system of differential equations 2.1, the points of equilibrium are sought. A system is said to be balanced, if the system no longer changes under certain conditions with time. To determine the equilibrium point of the equation system (2.1) is to make the rate of change of the system: \( \frac{dS}{dt} = 0 \), \( \frac{dl}{dt} = 0 \) and \( \frac{dR}{dt} = 0 \) are written:

\[
(1 - \sigma)\lambda N - b \frac{I}{N} S - \mu S = 0
\]

\[
\frac{b}{N} I S - (\mu + \delta)I = 0
\]

\[
\delta I + \lambda \sigma N - \mu R = 0
\]

Suppose: \( S = \frac{S}{N} \); \( I = \frac{I}{N} \); \( R = \frac{R}{N} \)

The equation system becomes:

\[
(1 - \sigma)\lambda - bsi - \mu s = 0
\]

\[
bsi - (\mu + \delta)i = 0
\]

\[
\delta i + \lambda \sigma - \mu r = 0
\]

3.1 Disease-Free Equilibrium Point (\( E_0 \)).

The first equilibrium point is the disease-free equilibrium point, where at this point the infected sub-population does not exist \( (i = 0) \). From equation (2.2) for disease-free state \( (i = 0) \), the equilibrium point is obtained:

\[
(1 - \sigma)\lambda - bsi - \mu s = 0
\]

\[
(1 - \sigma)\lambda - \mu s = 0
\]

\[
s^* = \frac{(1 - \sigma)\lambda}{\mu - \mu_t} = \frac{\sigma}{\mu}
\]

So that the disease-free equilibrium point is obtained:

\[
E_0(s^*, i^*, r^*) = \left( \frac{(1 - \sigma)\lambda}{\mu}; 0; \frac{\sigma}{\mu} \right)
\]
At the disease-free equilibrium point \((E_0)\) it is clear that the susceptible sub-population is \(\frac{(1-\sigma)\lambda}{\mu}\), while the infected sub population is not \(0\) and the recover sub population is \(\frac{\sigma\lambda}{\mu}\).

### 3.2 Endemic Equilibrium Point \((E_1)\)
In the same way to determine the endemic balance point.

For \(s^* = \frac{\delta + \mu}{b - t}\) and \(r^* = \frac{\delta(1-\sigma)\lambda + \mu\delta + \lambda\sigma(\delta + \mu)}{(\delta + \mu)\mu}\)

From equation (2.4) furthermore, if \(i \neq 0\) or \(i > 0\) means that there is already an infected sub population, which indicates that the infected sub population is likely to transmit TB disease to other individuals. So that the endemic balance points are obtained:

\[
E_1(s^*, i^*, r^*) = \left(\frac{\delta + \mu}{b - t}; \frac{(1-\sigma)\lambda + \mu\delta}{\delta + \mu}; \frac{\delta(1-\sigma)\lambda + \mu\delta + \lambda\sigma(\delta + \mu)}{(\delta + \mu)\mu}\right)
\]

### 3.3 Basic Reproduction Number Ratio \((R_0)\)
The basic reproduction number \((R_0)\) is a number which states the average number of secondary infective individuals as a result of being infected by primary infective individuals who take place in a susceptible population. In epidemiology, the level of spread of an infectious disease is usually measured by a value called the basic reproduction ratio \((R_0)\). To be free from TB infection, they must be made \(R_0 < 1\). Based on the dynamic system, if \(R_0 < 1\), the number of infected individuals will decrease monotonically towards \(0\), whereas if \(R_0 > 1\), the number of infected individuals will increase first [8]. In this case each patient can only spread the disease to an average of less than one new sufferer, so that in the end the disease will disappear. Meanwhile, if \(R_0 > 1\) then each patient can spread the disease to an average of more than one new sufferer, so that in the end there will be an epidemic.

Through the Next Generation matrix method, the reproduction number ratio can be determined by considering the differential equation in the infected subpopulation:

\[
\frac{di}{dt} = bis - (\delta + \mu)i
\]

Express:

\[
\theta = [bsi] \text{and } P = [(\delta + \mu)] \text{with linearization obtained:}
\theta = [bs - bi] \text{and } P = [(\delta + \mu)] \text{and } P^{-1} = \frac{1}{(\delta + \mu)}
\]

\[
K = FV^{-1} = R_0 = \frac{bs - bi}{(\delta + \mu)} \text{where } \frac{(1-\sigma)\lambda}{\mu} \text{ so } R_0 = \frac{b(1-\sigma)\lambda}{\mu(\delta + \mu)}
\]

Basic Reproduction Number Ratio is:

\[
R_0 = \frac{b(1-\sigma)\lambda}{\mu(\delta + \mu)}
\]

From the formula Basic reproduction number Ratio shows that the controllable parameter is the parameter vaccines through the administration of vaccines and the rate of recovery by providing therapy or drugs. From this formula to achieve \(R_0 < 1\) is obtained if:

\[
\sigma > 1 - \frac{\mu(\delta + \mu)}{b\lambda} \text{ or } \delta > \frac{b(1-\sigma)\lambda}{\mu} - \mu
\]

### 3.4 Simulation
Based on parameter values and existing data, model simulation is done using software MATLAB. The initial requirement used in this model simulation is based on the number of tuberculosis cases in the province of North Sumatra. The data were obtained from the North Sumatra Provincial Health Office and from the North Sumatra Central Bureau of Statistics.

The initial conditions that will be used in the simulation of this model are to determine the values of \(S(0), I(0), R(0), \mu, b, \delta \text{ and } \sigma\)
Table 2. Values of Variables and Parameters in the Disease SIR model simulation *Tuberculosis*

| No. | Variable / Parameter | Value   |
|-----|----------------------|---------|
| 1.  | $S(0)$              | 0.9980  |
| 2.  | $I(0)$              | 0.0019  |
| 3.  | $R(0)$              | 0.0001  |
| 4.  | $\mu$               | 0.0145  |
| 5.  | $\sigma$            | (0 – 1) |
| 6.  | $\lambda$           | 0.014   |
| 7.  | $b$                 | (0 - 1)$|
| 8.  | $\delta$            | 0.27    |

(1) Fredelina, Bagus and Eka, M., [7]

3.4.1 *For $R_0 < 1$*

For $R_0 < 1$ is also called a disease-free condition where the number of infected population does not exist ($I = 0$). Since there is no infection population, this condition can be achieved if the value of the parameters: $S(0)=0.9980; I(0) = 0.0019; R(0) = 0.0001; \lambda = 0.014; \mu = 0.0145; b = 0.04; \delta = 0.027; \sigma = 0$

![Figure 3. Chart the Spread of Tuberculosis SIR Models with $R_0 < 1$](image)

The graph in Figure 3, the Susceptible sub-population, does not show a significant decrease because in this condition it is a disease-free condition, where the infection sub-population does not exist or is equal to zero, as a result, sub-pollution is also zero healed. The graph clearly shows the I and R coincide over time in a population of zero.

3.3.2 *For $R_0 > 1$ without Vaccine.*

In a condition $Ro > 1$ is called an endemic condition, meaning that each patient can spread the disease to an average of more than one new patient so that in the end there will be an epidemic, this condition has an infection sub-population as a result of the healed sub-population also already exists. This section shows a graph with a $R_0 > 1$ state without vaccine. In this case the parameter values are taken: $S(0)=0.9980; I(0) = 0.0019; R(0) = 0.0001; \lambda = 0.014; \mu = 0.0145; b = 0.25; \delta = 0.027; \sigma = 0$
Figure 4. Chart the Spread of Tuberculosis SIR Models without Vaccine

The graph in Figure 4 is a graph with endemic conditions without vaccines, this graph shows that the decline in the Susceptible sub-population shifting to sub-infection infections is very significant over time. The number of infected subpopulation reaches its highest point when t is around 45 and the value is around 62%.

3.4.3 For $R_0 > 1$ with Vaccine
In this section, the condition $R_0 > 1$ with the vaccine. Vaccine performed on susceptible subpopulations. Assuming that every individual who is vaccinated will not be infected or enter the sub-population immediately recover. While those who have not been vaccinated enter the Susceptible sub-population. In this case the infected sub population and the recovered sub population also exist.

The following parameters are used in this condition: $S(0)=0.9980; I(0) = 0.0019; R(0) = 0.0001; \lambda = 0.014; \mu = 0.0145; b = 0.25 ; \delta = 0.027 ; \sigma = 0,1$

Figure 5. Chart the Spread of Tuberculosis SIR Models with Vaccine

The graph in Figure 5, is a graph of the dynamics of the spread of Tuberculosis with the effect of vaccines for conditions $R_0 > 1$ or also known as endemic conditions. In this section, the provision of vaccines to the susceptible sub-population of $\sigma = 0.1$ has an effect on slowing the spread of tuberculosis in the sub-population. The difference between the graph without vaccine and the graph with the vaccine is quite clear, the number of infected population at the same time shows different values. In the model without vaccine, the number of infected population is more than in the vaccine giving model. For endemic conditions, the administration of the vaccine at $\sigma = 0.1$ has not shown a big effect on the endemic, the infected sub population is still there (around 0.25) resulting in the possibility of transmission of Tuberculosis disease continuing. To make this endemic condition
become disease-free $R_0 < 1$, vaccine administration must be increased so that the number of infected population stabilizes to zero.

![Figure 6. Chart the Spread of Tuberculosis SIR Models with Vaccine $\sigma = 0.85$](image)

The graph in Figure 6 is a graph showing the dynamics of the spread of Tuberculosis after vaccine administration at $\sigma = 0.85$. This increase in vaccine administration results in a $R_0 < 1$ value achieved when the sub-population of the infection is stable towards zero, which can be achieved when $t > 180$. It is clear that vaccine administration will significantly slow down the growth of the infected population even with a change in the parameter value to $\sigma = 0.8$ can change the endemic state to a disease free state.

4. Conclusion

The spread of tuberculosis in the SIR model with vaccines provides two equilibrium points, namely a disease-free equilibrium point and an endemic equilibrium point. Through the analysis of the model, it is obtained the reproductive number ratio $R_0 = \frac{b(1-\sigma)\lambda}{\mu(\delta+\mu)}$. If $R_0 < 1$ is called a disease-free condition and if $R_0 > 1$ is called an endemic condition, a condition in which Tuberculosis continues to spread. Vaccines are very influential on the dynamics of the spread of Tuberculosis, as seen from the simulation results carried out with vaccines and without vaccines. Vaccination will slow down the growth of infection. The more population that is vaccinated, the more likely it is that the population is not infected. Therefore, vaccines are very suitable to prevent the spread of tuberculosis.

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