Model of transmission of three types Leprosy Disease with treatment

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Abstract. Leprosy disease is caused by infection of *Mycobacterium leprae* that affects the skin and nerve. The treatment duration for leprosy takes 6 to 24 months with multi-drug therapy. In this article, a 6-d mathematical model for transmission of three types leprosy disease with treatment was constructed. Analysis and numerical simulation were done to explore the existence and stability of equilibrium points and basic reproduction number $R_0$. The local stability of endemic equilibrium point was done by numerical simulation. Numerical simulation also confirmed that the disease-free equilibrium is locally asymptotically stable when $R_0 < 1$ and the endemic equilibrium point locally asymptotically stable when $R_0 > 1$. Numerical simulation was also done to show the sensitivity of $R_0$ with respect to some contact parameters. The result showed that the change of contact rate between susceptible people and lepromatous type infected hosts has more effect to change the value of $R_0$. The reduction of contact rate between susceptible people and lepromatous type infected hosts is more effective to control prevention leprosy disease compared with tuberculoid and borderline types.

Keywords: Basic reproduction number, differential equation system, equilibrium point, leprosy, mathematical model.

1. Introduction
Leprosy or Morbus Hansen is a disease that has long time incident since ancient times. It was noted in the Papyrus document in Egypt which written about 1550 BC [1]. Leprosy patient in all history always misconstrued and feared until 1873. In 1873, dr. Gerhard Armauer Henrik Hansen finally found the main cause of leprosy disease, which is *Mycobacterium leprae*. The treatment for leprosy patients uses multi-drug therapy (MDT) which consists of *dapsone*, *rifampicin*, and *clofazimine*. Ridley-Jopling classification of leprosy was made based on clinical spectrum, bacteriology, and immunology. The classification consists of five types of leprosy, those are tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL), lepromatous (LL) [2, 3].

Data from the World Health Organization (WHO) in 2012 showed that there were 232,857 people affected by leprosy worldwide. Indonesia is the third country with the largest number of people affected by leprosy, which is 18,994 (8.16 % of the total infected people in the world) after India (134,752 infectives) and Brazil (33,303 infectives) [4].

Mathematical modelling of the spread of leprosy has been carried out by some researchers. Chiyaka focused on modelling 2 types of leprosy [5]. Neima explored on the important factors of leprosy using mathematical model [6]. Smith focused on parameterizing for the spread leprosy disease in Brazil [7].
Smith discussed mathematical modelling of two types of leprosy based on WHO classification, namely type paucibacillary and multibacillary types. In this article mathematical modelling of three types of leprosy with treatment was done. The constructed model is a modification of the model made by Chiyaka. Three types of leprosy considered in this article are tuberculoid, lepromatous, and borderline. We assume that borderline tuberculoid, mid borderline, and borderline lepromatous were grouped into one group because the case the three cases are rare.

2. Experimental method
In this article mathematical modelling for leprosy disease used SEIR (susceptible, exposed, infection, recovery) approach. The model is a system of six ordinary differential equations. Then the model was analyzed to find equilibrium points, stability of the equilibrium points, and basic reproduction number. There are two approaches for the model in this article. The first one is analytical analysis. From the analysis, it was found the condition for existence and stability of the disease-free equilibrium, basic reproduction number and the existence of endemic equilibrium. The second one is numerical simulation. From the numerical simulation, we found the stability of endemic equilibrium and the sensitivity of basic reproduction ratio with respect to contact rates.

3. Results and discussion

3.1. Model construction
The assumptions used in the model are as follows the human population is homogeneous and constant. The borderline tuberculoid (BT), mid borderline (BB) and borderline lepromatous (BL) types of tuberculosis were merged into borderline type. The leprosy treatment follows the doctor’s prescription either dosage or treatment duration and no resistance of bacteria to leprosy drug. The infection occurs between susceptible people and infected people. There is no migration. The per capita rate of birth is equal to the per capita rate of death. Someone who is cured of leprosy can be infected leprosy again.

We used six variables as following. Variable $S$ is the number of susceptible hosts, $E$ is the number of people exposed to leprosy, $M$ is the number of people infected by lepromatous (LL) type, $B$ is the number of people infected by borderline type, $P$ is the number of people infected by tuberculoid type, $R$ is the number of people recovered from leprosy. Figure 1 illustrates the transmission diagram of the three types of leprosy. Meanwhile, table 1 shows the parameters used in the modelling.

![Figure 1. Transmission and transition diagram of leprosy disease.](image-url)
Table 1. Parameter list

| Parameter | Description | Value | Unit |
|-----------|-------------|-------|------|
| $\mu$     | Rate of per capita birth and rate of per capita death. | 0.01426 | 1/year |
| $\epsilon$ | Per capita rate of immunity decreases from recovered hosts to susceptible person. | 1 | 1/year |
| $\kappa$ | Per capita rate of transition from one type leprosy to other type of leprosy. | 4.56 | 1/year |
| $\alpha_1$ | Per capita rate of transition from exposed hosts to LL type leprosy infected hosts. | 0.1 | 1/year |
| $\alpha_2$ | Per capita rate of transition from exposed hosts to Borderline type leprosy infected hosts. | 0.19 | 1/year |
| $\alpha_3$ | Per capita rate of transition from exposed hosts to tuberculoid type infected hosts. | 0.28 | 1/year |
| $\beta_1$ | Per capita contact rate of susceptible hosts and LL type infected hosts. | $\beta_1 \geq 0$ | 1/year |
| $\beta_2$ | Per capita contact rate of susceptible hosts and Borderline type infected hosts. | $\beta_2 \geq 0$ | 1/year |
| $\beta_3$ | Per capita contact rate of susceptible hosts and tuberculoid type infected hosts. | $\beta_3 \geq 0$ | 1/year |
| $\delta_1$ | Per capita treatment rate of LL type hosts. | 1 | 1/year |
| $\delta_2$ | Per capita treatment rate of borderline type hosts. | 1.5 | 1/year |
| $\delta_3$ | Per capita treatment rate of tuberculoid type hosts. | 2 | 1/year |

Based on the assumptions, transmission diagram in figure 1 and parameters in table 1, the transmission model of three types leprosy with treatment is as following.

$$\frac{dS}{dt} = \mu N + \epsilon R - \mu S - \frac{\beta_1 SM}{N} - \frac{\beta_2 SB}{N} - \frac{\beta_3 SP}{N},$$

$$\frac{dE}{dt} = \frac{\beta_1 SM}{N} + \frac{\beta_2 SB}{N} + \frac{\beta_3 SP}{N} - \alpha_1 E - \alpha_2 E - \alpha_3 E - \mu E,$$

$$\frac{dM}{dt} = \alpha_1 E + \kappa B - \mu M - \delta_1 M,$$

$$\frac{dB}{dt} = \alpha_2 E - \kappa B - \mu B - \delta_2 B + \kappa P,$$

$$\frac{dP}{dt} = \alpha_3 E - \kappa P - \mu P - \delta_3 P,$$

$$\frac{dR}{dt} = \delta_1 M + \delta_2 B + \delta_3 P - \mu R - \epsilon R.$$

(1)

where $N = S + E + M + B + P + R$. Parameter $N$ is the total population.
3.2. Analysis
A disease-free equilibrium is a condition where there is no disease in population. In our context, the population is leprosy-free. The disease-free equilibrium of model 1 is \(DFE = (S, E, M, B, P, R) = (N, 0, 0, 0, 0, 0)\).

Basic reproduction number \(R_0\) is defined as the number of secondary infections generated by a primary infected individual during his/her infectious period in a susceptible population. Basic reproduction number is obtained through the next generation matrix method \([8, 9]\). The basis reproduction number \(R_0\) of model 1 is,

\[
R_0 = \frac{k^2 \alpha_3 \beta_1 + k \omega \alpha_3 \beta_2 + k \gamma \alpha_2 \beta_1 + w \gamma \alpha_3 \beta_3 + w \gamma \alpha_2 \beta_2 + y \gamma \alpha_1 \beta_1}{xwyz} \tag{2}
\]

where \(w = \mu + \delta_1\), \(x = \mu + \alpha_1 + \alpha_2\), \(y = \kappa + \mu + \delta_2\), and \(z = \kappa + \mu + \delta_3\).

An endemic equilibrium is a condition which a disease is endemic in population. Here, \(E \neq 0, M \neq 0, B \neq 0, P \neq 0\). The endemic equilibrium point of model 1 is \(EE = (S^*, E^*, M^*, B^*, P^*, R^*)\), where,

\[
S^* = \frac{((\delta_2 z \alpha_2 + \alpha_3 (k \delta_2 + y \delta_3))w + ((\kappa \alpha_2 + y \alpha_1)z + k^2 \alpha_3) \delta_1)E^* + \mu N z w y v}{((\beta_2 \alpha_2 z + \alpha_3 (k \beta_2 + y \beta_3))w + ((\kappa \alpha_2 + y \alpha_1)z + k^2 \alpha_3) \beta_1)E^* + \mu N z y w}, \tag{3}
\]

\[
E^* = -\frac{x w y z^2 \mu N}{q}, \quad M^* = \frac{E^*(k^2 \alpha_3 + k \alpha_2 + y \alpha_1)}{zyw}, \quad B^* = \frac{E^*(k \alpha_2 + z \alpha_2)}{zy}, \tag{3}
\]

\[
P^* = \frac{E^* \alpha_3}{z},
\]

\[
R^* = \frac{((\delta_2 z \alpha_2 + \alpha_3 (k \delta_2 + y \delta_3))w + ((\kappa \alpha_2 + y \alpha_1)z + k^2 \alpha_3) \delta_1)E^*}{zyw}
\]

and \(v = \mu + \epsilon\). The endemic equilibrium \(EE\) exists if \(R_0 > 1\).

The disease-free equilibrium \(DFE\) is locally asymptotically stable if \(R_0 < 1\). We found that the endemic equilibrium \(EE\) is locally asymptotically stable using numerical experiment.

3.3. Numerical simulation
Figure 2a shows the sensitivity analysis of \(R_0\) with respect to parameter \(\beta_1\). Here, \(\beta_2\) and \(\beta_3\) are set fixed at 0.5. If \(\beta_1\) increases 1 unit then \(R_0\) increases 0.64. The result of sensitivity analysis of \(R_0\) with respect to parameter \(\beta_2\) (with \(\beta_1 = \beta_3 = 0.5\)) could be seen in figure 2b. If \(\beta_2\) increases 1 unit then \(R_0\) increases 0.108. Meanwhile, figure 2c showed the sensitivity analysis of \(R_0\) with respect to parameter \(\beta_3\) (with \(\beta_1 = \beta_2 = 0.5\)). If \(\beta_3\) was increased 1 unit then \(R_0\) increased 0.073. From these three sensitivity analysis experiments of \(R_0\), the susceptible population has higher probability to be infected if doing contact with LL infected hosts compared with the borderline, or tuberculoid infected hosts.

Figure 3a shows the phase portrait of susceptible population \(S\) and exposed population \(E\). We used \(N = 10,000\), \(R_0 = 0.5\), and three initial points. The number of susceptible population \(S\) tends to 10,000 and the exposed population \(E\) is going to 0. Thus, when \(R_0 < 1\) the population tends to the disease-free equilibrium \(DFE\).

Figure 3b shows the phase portrait of susceptible population \(S\) and exposed population \(E\) where \(N = 10,000\) and \(R_0 = 2\). We also used three initial points for simulation. The number of susceptible population \(S\) tends to 5,000 and the exposed population \(E\) tends to 2,446. So, when \(R_0 > 1\) the population tends to the endemic equilibrium \(EE\).
Dynamics of susceptible population $S$ and exposed $E$ with various values of parameter $\beta_1$ are given in figure 4a and figure 4b respectively. When the value of parameter $\beta_1$ increases, then the number of susceptible population $S$ decreases but the number of exposed population $E$ increases. From the simulation, when the value of parameter $\beta_1$ increases from 1.0 to 2.0, the number of susceptible population $S$ drops almost 30%.

Meanwhile, the dynamics of susceptible population $S$ and exposed $E$ with various values of parameter $\beta_2$ are given in figure 5a and figure 5b respectively. When the value of parameter $\beta_2$ increases, then the number of susceptible population $S$ decreases but the number of exposed population $E$ increases. From the simulation, when the value of parameter $\beta_2$ increases from 4.0 to 7.0, the number of susceptible population $S$ drops almost 25%.

Moreover, the dynamics of susceptible population $S$ and exposed $E$ with various values of parameter $\beta_3$ are given in figure 6a and figure 6b respectively. When the value of parameter $\beta_3$ increases, then the number of susceptible population $S$ decreases but the number of exposed population $E$ increases. From the simulation, when the value of parameter $\beta_3$ increases from 6.0 to 12.0, the number of susceptible population $S$ drops almost 25%.
4. Conclusion
In this article, a mathematical model for leprosy spread was constructed. The model incorporated three types of leprosy and treatment intervention. The model has disease-free equilibrium point and endemic equilibrium point. The existence and local stability of the points depend on basic reproduction ratio.

The value increment of per capita contact rate of susceptible people with LL infected hosts, borderline infected hosts, or tuberculoid infected hosts will make the population tends to the endemic equilibrium. It means leprosy can spread faster if more frequent contact with leprosy infected hosts. So, if there are some people who have leprosy disease, that people must get treatment quickly.
Acknowledgments
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