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AARJMD ASIAN ACADEMIC RESEARCH JOURNAL OF MULTIDISCIPLINARY MATHEMATICAL MODEL FOR CONTROLING OF THE SPREADS OF PULMONARY TUBERCULOSIS (TB) DISEASE BUYUNG KERAMAN[1]; MUHAM....

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MATHEMATICAL MODEL FOR CONTROLING OF THE SPREADS OF PULMONARY TUBERCULOSIS (TB) DISEASE

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Abstract

Pulmonary Tuberculosis (TB) is one of common diseases in developing countries, especially in communities of low economic and poor nutrition status, it can cause death. Therefore, it is necessary to analyze the spreads of tuberculosis, one of them is to formulate a mathematical model of the spread of TB. The mathematical model of the spreads of TB is arranged into four groups (communities); susceptible (S), latent (L), infectious (I) and recovered (R). Models created are analyzed by finding TB disease-free equilibrium point and TB endemic equilibrium point. Controling the spreads of TB disease needs to minimize its spreads in each group and to control patients who have been declared recovery and not reinfected in the future.

Keywords: Mathematical Model, Tuberculosis (TB), a disease-free equilibrium point of TB, endemic equilibrium poin of TB.

1. Introduction

Tuberculosis (TB) is one of the causes of the death in developing countries which caused by mycobacterium. The symptoms of TB include coughing, chest pain, shortness of breath, loss of appetite, weight loss, fever, chills and fatigue.

Based on data of the World Health Organization (WHO) in 2007, Indonesia ranked third that became after India and China, in 2009 Indonesia shifted down to fifth after India, China, South Africa and Nigeria. WHO reported on the global total TB cases in Indonesia was 294.731 cases (WH0, 2010).

To reduce the prevalence of TB in Indonesia in 1995 the WHO recommended DOTS strategy (Directly Observed Treatment Short-course) be implemented in all health care units supported by active participations of various stakeholders, and performed a variety of specific activities in accordance with local innovations.

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Study to find the problem solving of the spreads of TB has been widely applied, including quantitative method approaches through mathematical model. In the last 10 years, a lot of research for the mathematical model of the spread of pulmonary TB has been done.

To determine the mathematical model of the spreads of TB disease in a community, the population is divided into 4 groups/classes: **Susceptible (S(t))** is a group that is vulnerable to pulmonary tuberculosis at time t, **Latent (L(t))** is stated the individual numbers were detected pulmonary tuberculosis but had not yet infected others, it means medically symptoms of pulmonary TB disease has not been developing at time t, **Infectious (I(t))** is stated the individual numbers that infected with pulmonary TB and could infect other people (contacts) at time t and **Recovered (R(t))** is stated the individual numbers who had recovered at time t.

The mathematical model established is a mathematical model which is built in the form of differential equations depending on the variables exist in each group/class. Waaler et al. (1962) was the first mathematician constituted modeling TB disease using discrete differential equation system. The study was later developed by Adetune (2007) by addressing the dynamic behavior of TB disease. In this paper, a mathematical model formulation of TB which is discussed in detail and searches the disease-free equilibrium and the endemic equilibrium point as well as controls patients who had recovered from TB and they have not reinfection.

2. Formulation Model

In the establishment of a mathematical model in controling the spread of TB, the population is divided into 4 groups: susceptible (S (t)), Latent (L (t)), Infectious (I (t)) and recovered (R (t)), so that the symbols and parameters used in the models are as follows:

Table 1. Symbols and parameters of the models

Symbols	Parameters of the Models

From symbols and parameters above, they can be made compartment diagrams of mathematical models of TB as follows:

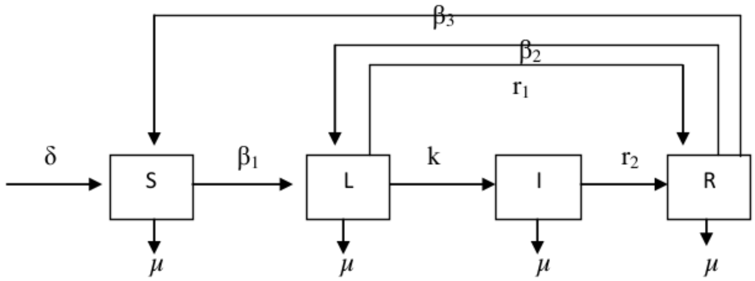


Figure 1. Flowchart of Mathematical Models

Based on Figure 1 above, the mathematical models of the spreads of tuberculosis are:

$$\frac{dS}{dt} = \delta - \mu S - \beta_1 cS\frac{I}{A} + \beta_3 cR\frac{I}{A} \quad \textbf{(1a)}$$

$$\frac{dL}{dt} = \beta_1 cS\frac{I}{A} - (\mu + k + r_1)L + \beta_2 cR\frac{I}{A} \quad \textbf{(1b)}$$

$$\frac{dI}{dt} = kL - (\mu + r_2)I \quad \textbf{(1c)}$$

$$\frac{dR}{dt} = r_1 L + r_2 I - \mu R - \beta_2 cR\frac{I}{A} - \beta_3 cR\frac{I}{A} \quad \textbf{(1d)}$$

Where A represents the total area and N = S + L + I + R is the total population size.

3. **Analysis of Mathematical Models**

3.1. The disease-free equilibrium point and endemic

To figure out the system balance point of differential equations (1a-1d) such as the disease-free equilibrium point and endemic, system (1a-1d) made in a constant position with respect to time is a condition in which obtained two balance points as follows:

3.1.1. The disease-free equilibrium point

Lemma 1:

If I = 0 means there is no individuals infected and transmited TB to other individuals, then the system of differential equations (1a-1d) has a disease-free equilibrium point, $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$

Evidence:
Consider the system of differential equations (1a-1d).
If the right-hand side of each system of differential equations (1a-1d) is made equal to zero and assumed that there is no individuals infected germs of Tuberculosis (TB) means I = 0, then we obtain:

$\frac{dS}{dt} = 0$ *or* $\delta - \mu S = 0$ or $\mathbf{S} = \frac{\delta}{\mu}$

$\frac{dL}{dt} = 0$ *or* $L = 0$ and

$\frac{dR}{dt} = 0$ *or* $R = 0$ in this case written $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$

means that the population is free from pulmonary tuberculosis (TB).

3.1.2. endemic equilibrium point

Lemma 2

If I≠0 means there are individuals who are infected and transmit TB to other individuals, then the system of differential equations (1a-1d) has endemic equilibrium point $E_1 = (I^*, L^*, I^*, R^*)$ where is $(I^*, L^*, I^*, R^*) \neq 0$.

Evidence
Consider the system of differential equations (1a-1d)
If the right-hand side of each system of differential equations (1a-1d) assumed equal to zero and there are individuals who are infected with pulmonary TB (I≠0), then we obtain:

From equation (1c)

$$\frac{dI}{dt} = 0 \text{ or } kL - (\mu + r_2)I = 0$$

$\Longleftrightarrow$

$L = \frac{\mu+r_2}{k} I$ (2)

from the equation (1d)

$\frac{dR}{dt} = 0 \;\; atau \;\; r_2 I + r_1 L - \mu R - \beta_2 c R\left(\frac{I}{A}\right) + \beta_3 c R\left(\frac{I}{A}\right) = 0$ wherein $(\beta_3 = 1 - \mu - \beta_2)$

$\Longleftrightarrow r_2 I + r_1\left[\frac{(\mu+r_2)I}{k}\right] - \left[\mu + \beta_2 c\left(\frac{I}{A}\right) + \beta_3 c\left(\frac{I}{A}\right)\right] R = 0$

$\Leftrightarrow$ **R** $= \frac{[kr_2+r_1(\mu+r_2)]}{kc(\mu+\beta_2+\beta_3)\left(\frac{I}{A}\right)} I$ (3)

from the equation (1a)

$\frac{dS}{dt} = 0 \; atau \; \delta - \mu S - \beta_1 c S\left(\frac{I}{A}\right) + \beta_3 c R\left(\frac{I}{A}\right) = 0$

$\Longleftrightarrow \;\; \delta - \left[\mu + \beta_1 c\left(\frac{I}{A}\right)\right] S + \beta_3 c\left\{\frac{[kr_2+r_1(\mu+r_2)]I}{kc(\mu+\beta_2+\beta_3)\left(\frac{I}{A}\right)}\right\}\left(\frac{I}{A}\right) = \mathbf{0}$

$\Leftrightarrow$ **S** $= \frac{\delta kc(\mu+\beta_2+\beta_3)+\beta_3 c\{[kr_2+r_1(\mu+r_2)]I\}}{kc(\mu+\beta_2+\beta_3)\left(\mu+\beta_1 c\left(\frac{I}{A}\right)\right)}$ (4)

If equation of (2), (3) and (4) is substituted in equation $\frac{dL}{dt} = 0$, it is obtained

$\beta_1 c S \frac{I}{A} - (\mu + k + r_1) L + \beta_2 c R \frac{I}{A} = 0$

$\{\beta_1\beta_3 c[kr_2 + r_1(\mu + r_2)] + \beta_1 c(\mu + r_1 + k)(\mu + r_2)(\mu + \beta_2 + \beta_3) + \beta_1 c\beta_2[kr_2 + r_1(\mu + r_2)]\} I^2 - \{A\mu(\mu + r_1 + k)(\mu + r_2)(\mu + \beta_2 + \beta_3) - \mu A\beta_2[kr_2 + r_1(\mu + r_2)] - \beta_1\delta kc(\mu + \beta_2 + \beta_3)\} I = 0$

$\Leftrightarrow$

I
{

$$I\{\beta_1\beta_3 c[kr_2+r_1(\mu+r_2)]+\beta_1 c(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)+\beta_1 c\beta_2[kr_2+r_1(\mu+r_2)]\}-\{A\mu(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)-\mu A\beta_2[kr_2+r_1(\mu+r_2)]-\beta_1\delta kc(\mu+\beta_2+\beta_3)\}=0$$

Or it can be written: $a_0 I^2 + a_1 I = 0$ with

$a_0 =$

$$\beta_1\beta_3 c[kr_2+r_1(\mu+r_2)]+\beta_1 c(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)+\beta_1 c\beta_2[kr_2+r_1(\mu+r_2)]$$

and

a_1=-{

$$A\mu(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)-\mu A\beta_2[kr_2+r_1(\mu+r_2)]-\beta_1\delta kc(\mu+\beta_2+\beta_3)\}$$

that obtained the roots of a quadratic equation in I is

$I_1 = 0$

and

$$\mathbf{I_2} = \frac{\{A\mu(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)-\mu A\beta_2[kr_2+r_1(\mu+r_2)]-\beta_1\delta kc(\mu+\beta_2+\beta_3)\}}{\beta_1\beta_3 c[kr_2+r_1(\mu+r_2)]+\beta_1 c(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)+\beta_1 c\beta_2[kr_2+r_1(\mu+r_2)]}$$

The endemic equilibrium point is $E_1 = (S^*, L^*, I_2^*, R^*)$ with

$$S^* = \frac{\delta kc(\mu+\beta_2+\beta_3)+\beta_3 c\{[kr_2+r_1(\mu+r_2)]I\}}{kc(\mu+\beta_2+\beta_3)\left(\mu+\beta_1 c\left(\frac{I}{A}\right)\right)},$$

$$\mathbf{L^*} = \frac{\mu+r_2}{k}\,\mathbf{I}$$

$$\mathbf{I^*} = \frac{\{A\mu(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)-\mu A\beta_2[kr_2+r_1(\mu+r_2)]-\beta_1\delta kc(\mu+\beta_2+\beta_3)\}}{\beta_1\beta_3 c[kr_2+r_1(\mu+r_2)]+\beta_1 c(\mu+r_1+k)(\mu+r_2)(\mu+\beta_2+\beta_3)+\beta_1 c\beta_2[kr_2+r_1(\mu+r_2)]}$$

$$R^* = \frac{[kr_2+r_1(\mu+r_2)]I}{kc(\mu+\beta_2+\beta_3)\left(\frac{I}{A}\right)}$$

3.2. Eigen Values

Eigen value serves to determine the stability of a system, to find out the Eigen values that need to be done is to figure out the Jacobian matrix (J). Jacobian matrix of the system (1a-1d) is JE1 as follows:

$$J_{E1}=\begin{pmatrix} -\mu-\beta_1 c\frac{I}{A} & 0 & -\beta_1 c\frac{S}{A}+\beta_3 c\frac{R}{A} & \beta_3 c\frac{I}{A} \\ \beta_1 c\frac{I}{A} & (\mu+k+r_1) & \beta_1 c\frac{S}{A}+\beta_2 c\frac{R}{A} & \beta_2 c\frac{I}{A} \\ 0 & k & -(\mu+r_2) & 0 \\ 0 & r_1 & r_2-\beta_2 c\frac{R}{A} & -(\mu+\beta_2 c\frac{I}{A}+\beta_3 c\frac{I}{A}) \end{pmatrix}$$

By substituting the value of $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$ in the J_{E1} matrix obtains the Jacobian matrix for J_{Eo} as follows:

$$JE_0=\begin{pmatrix} -\mu & 0 & -\beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & -(\mu+r_1+k) & \beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & k & -(\mu+r_2) & 0 \\ 0 & r_1 & r_2 & -\mu \end{pmatrix}$$

3.3. Minimizing/controling of the spreads of pulmonary tuberculosis disease

Will be investigated the stability of equilibrium point $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$, before that will be given Routh Hurwitz criterion as follows.
Routh Hurwitz theorem (Eminugroho, 2010)

All the roots of the polynomial matrix A,

$P_A(\lambda) = a_0\lambda^n + b_0\lambda^{n-1} + a_1\lambda^{n-2} + b_1\lambda^{n-3} + \ldots$, having negative real parts if and only if it satisfies:

$a_o\Delta_{1>0}$, $ao\Delta_2 > 0$, $ao\,\Delta_3 > 0, \ldots, ao\Delta_n > 0$, **for odd n ganjil dan** $\Delta_n > 0$, **for even n with**

$\Delta_1 = b_0$; $\Delta_2 = \det\begin{pmatrix} b_0 & b_1 \\ a_0 & a_1 \end{pmatrix}$; $\Delta_3 = det\begin{pmatrix} b_0 & b_1 & b_2 \\ a_0 & a_1 & a_2 \\ 0 & b_1 & b_2 \end{pmatrix}$ and so on.

Lemma 3.

Given matrix A_{2x2}

Real parts of all eigen values of matrix A have negative values if and only if the trace (A) <0 and det (A)> 0

Evidence:

In case of the matrix A = $\begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$, so that the characteristic polynomial is

$$|A-\lambda I| = \begin{vmatrix} a_{11}-\lambda & a_{12} \\ a_{21} & a_{22}-\lambda \end{vmatrix} = \lambda^2\text{-}(a_{11}+a_{22})\,\lambda + (\,a_{11}a_{22}.a_{12}a_{21}$$

From the polynomial above polynomial obtained $\mathbf{a_0=1}$ **;** $\mathbf{b_0= -(a_{11}+a_{22}) = -}$ **trace (A),** $\mathbf{a_1= a_{11}a_{22} - a_{21}a_{12}=}$**det(A) dan** $\mathbf{b_1 = 0}$.

Furthermore, by using the Routh Hurwitz theorem is obtained:

(1) $\mathbf{a_0\Delta_1 = a_0b_0 > 0}$

$\Leftrightarrow$ $\mathbf{b_0= -(a_{11}+a_{22}) >0}$

$\Leftrightarrow$ $\mathbf{b_0 = -}$ **trace (A) > 0**

$\Leftrightarrow$ **trace (A) < 0**

(2) $\mathbf{\Delta_2 > 0}$ **maka** $\Delta_2 = \begin{vmatrix} b_0 & b_1 \\ a_0 & a_1 \end{vmatrix} = \begin{vmatrix} -trace\ (A) & 0 \\ 1 & \det(A) \end{vmatrix}$ **= -trace (A).det (A) > 0**

Then det (A)> 0, because of (1) - trace (A)> 0.

Based on the above lemma, the following will discuss the stability of the equilibrium point E0 in the following lemma;

Lemma 4.

If $(\mu + r_1 + k)(\mu + r_2\ ) > k\,\beta_1 c\left(\frac{\delta/\mu}{A}\right)$, then the equilibrium point E_0 globally asymptotically stable.

Evidence:
Jacobian matrix of the system (1a-1d) is:

$$JE_1 = \begin{pmatrix} -\mu-\beta_1 c\frac{I}{A} & 0 & -\beta_1 c\frac{S}{A}+\beta_3 c\frac{R}{A} & \beta_3 c\frac{I}{A} \\ \beta_1 c\frac{I}{A} & (\mu+k+r_1) & \beta_1 c\frac{S}{A}+\beta_2 c\frac{R}{A} & \beta_2 c\frac{I}{A} \\ 0 & k & -(\mu+r_2) & 0 \\ 0 & r_1 & r_2-\beta_2 c\frac{R}{A} & -(\mu+\beta_2 c\frac{I}{A}+\beta_3 c\frac{I}{A}) \end{pmatrix}$$

by substituting the value of $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$ into the matrix of J_{E1} that the Jacobian matrix is around E_0 equilibrium point is

$$JE_0 = \begin{pmatrix} -\mu & 0 & -\beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & -(\mu+r_1+k) & \beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & k & -(\mu+r_2) & 0 \\ 0 & r_1 & r_2 & -\mu \end{pmatrix}$$

Characteristic polynomial of the Jacobian matrix is around the point E_0 namely

$$|JE_0 - \lambda I| = 0$$

$$\Leftrightarrow \begin{vmatrix} -\mu-\lambda & 0 & -\beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & -(\mu+r_1+k)-\lambda & \beta_1 c\left(\frac{\delta/\mu}{A}\right) & 0 \\ 0 & k & -(\mu+r_2)-\lambda & 0 \\ 0 & r_1 & r_2 & -\mu-\lambda \end{vmatrix} = 0$$

$$\Leftrightarrow (-\mu-\lambda)^2 \begin{vmatrix} -(\mu+r_1+k)-\lambda & \beta_1 c\left(\frac{\delta/\mu}{A}\right) \\ k & -(\mu+r_2)-\lambda \end{vmatrix} = 0$$

In case of the **B** matrix $= \begin{pmatrix} -(\mu+r_1+k) & \beta_1 c\left(\frac{\delta/\mu}{A}\right) \\ k & -(\mu+r_2) \end{pmatrix}$

Det (**B**) = $(\mu+r_1+k)(\mu+r_2) - k\,\beta_1 c\left(\frac{\delta/\mu}{A}\right)$ *and*

Trace (**B**) = $-(\mu+r_1+k)-(\mu+r_2)$, then the trace (B) <0 for all parameters, $\mu, k, r_1, r_2, \beta_1$, c and A positive.

Because it is known $(\mu + r_1 + k)(\mu + r_2) > k\,\beta_1 c\left(\frac{\delta/\mu}{A}\right)$, accordingly obtaining det **(B)=** $(\mu + r_1 + k)(\mu + r_2) - k\,\beta_1 c\left(\frac{\delta/\mu}{A}\right) > 0$.

Because det (B)> 0, then:

$\left(\frac{\delta/\mu}{A}\right) < \left(\frac{\mu+r_1+k}{k}\right)\left(\frac{\mu+r_2}{\beta_1 c}\right)$, So that the disease-free equilibrium point of E_0 is stable

$\left(\frac{A}{\delta/\mu}\right) > \left(\frac{k}{\mu+r_1+k}\right)\left(\frac{\beta_1 c}{\mu+r_2}\right)$ where $\left(\frac{A}{\delta/\mu}\right)$ is the area per individual.

$\left(\frac{k}{\mu+r_1+k}\right)$ is the possibility of survival of the latent into the infectious.

$\left(\frac{\beta_1 c}{\mu+r_2}\right)$ L is the number of infected group

To minimize the spread of TB in a group of individuals, in this case the numbers of the group of L and the group of I is reduced in number, when is $\frac{dL}{dt} < 0$ **and** $\frac{dI}{dt} < 0$. such as :

$$\beta_1 cS\left(\frac{I}{A}\right) - (\mu + k + r_1)L + \beta_2 cR\left(\frac{I}{A}\right) < 0 \qquad \textbf{(5)}$$

$$\textbf{and}\quad kL - (\mu + r_2)I < 0 \qquad \textbf{(6)}$$

from the inequality (6) is obtained:

$$I > \frac{kL}{\mu+r_2} \qquad (7)$$

from the inequality (5) is obtained:

$$A > \frac{(\beta_1 cS + \beta_2 cR)I}{(\mu+k+r_1)L} \qquad (8)$$

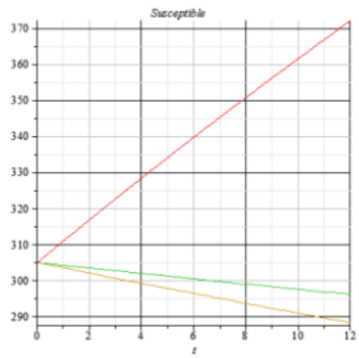
The combination of the inqequality (7) and (8) is obtained

$$A > \left\{\frac{k}{\mu+k+r_1}\right\}\left\{\frac{\beta_1 cS+\beta_2 cR}{\mu+r_2}\right\}$$

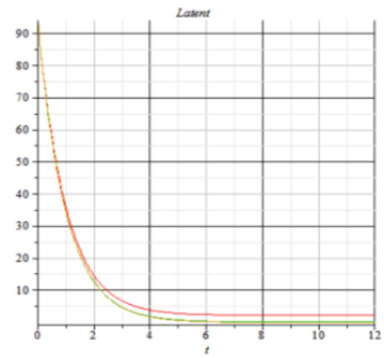
It means to minimize the occurrence of endemic diseases of pulmonary TB that the total area occupied by a particular group (A) must be greater than the individual life possibilities of the class detected TB (L) classes to become infected with TB (I) is $\left\{\frac{k}{\mu+k+r_1}\right\}$ as well as the number of infected individuals during the individuals are in the incubation period i.e. $\left\{\frac{\beta_1 cS+\beta_2 cR}{\mu+r_2}\right\}$.

4. **Simulation Mode**

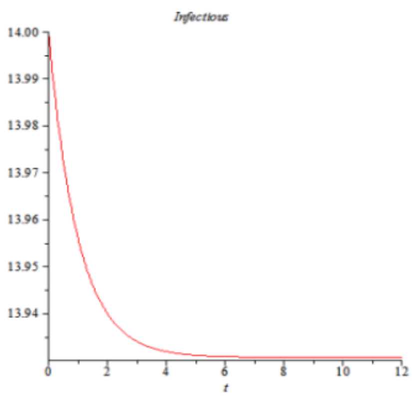
Here is given a simulation of the system 1 (1a-1d) using Maple program of parameter values are given as follows: δ = 0.016; μ = 0.005; β1 = β2 = 0.01; A = 20, 200 and 2000; I = 14; R = 14; β3 = 1-μ-β2 = 0.985; k = 0.14894; r1 = 0.85 and r2 = 1 with the initial condition S (0) = 305; L = 94;. By t = 12 months, Thus obtained:



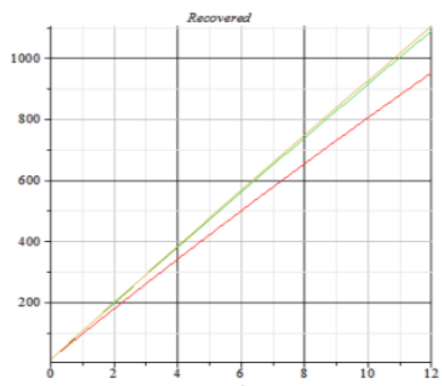
Picture 1: Susceptible (S)



Picture 2: Latent (L)



Picture 3: Infectious (I)



Picture 4: Recovered (R)

Considering Figure 1, when the residential area of 20 unit area (m2), the number of sub-populations that are vulnerable to a very fast growing of TB, this is indicated by the red graph. When the residential area of 200 unit area plus the number of sub-populations that are vulnerable to TB will be reduced (down), this is indicated by the blue graph, and when coupled residential area like 2000 unit wider then the number of sub-populations will be more susceptible to TB quickly reduced. This means fewer chances of TB infection, so the possibility of endemic TB will also be reduced. If the number of sub-populations that are vulnerable to TB slower decreasing (S population increases), the population is infected and detected with TB will be reduced as means TB disease can be minimized.

In the graph of sub-populations Latent (L) is a group that has been detected TB but has not yet infected others can be seen from the three groups, namely residential area A = 20, 200 and 2000 the differencs are not significant during the period of 12 months. It is due to 94 people who have been detected if no special treatment and no significant change of lifestyle are almost the same, they will be infected with positive TB BTA. However, specifically for the A = 20 L changes the number of sub-populations are slightly slower if they are compared with the change in the number of sub-populations to A = 200 and 2000.

For the case of sub-populations that have been infected with positive TB BTA totaled 14 people following the routine treatment for 6 months all are recovered evidently.

In the recovered (R) graph is seen that in the period t = 12 months all patients with positive TB BTA as many as 14 people. All declared cured after treatment for 6 months, it means that all patients who have been declared cured and rejoined the group of susceptible (S) subpopulations and this needs to be controlled so that people who have recovered are not entered into the group of Latent (L) or group of I called reinfection, it needs to be maximized β_3 and minimized β_2.

5. Conclusion

a. Being obtained two types of equilibrium that are disease-free equilibrium point $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$ and free endemic equilibrium point i.e. $E_1 = (S^*, L^*, I_2^*, R^*)$.

b. Pulmonary TB disease-free population at the time of the disease-free equilibrium point of pulmonary tuberculosis $E_o = (\frac{\delta}{\mu}, 0, 0, 0)$.

c. Minimizing the occurrence of endemic diseases of pulmonary TB, the total area habited by a particular group (A) have to be greater chances than the individual life of the class detected TB (L) classes to become infected with TB (I) is $\left\{\frac{k}{\mu+k+r_1}\right\}$ as well as the number of infected individuals during the incubation period is $\left\{\frac{\beta_1 cS+\beta_2 cR}{\mu+r_2}\right\}$.

d. Controling indiduals who are rocovered so that they do not have reinfection of tuberculosis with maximizing the value of β_3, to have the maximum value of β_3 that β_2 should be minimized to near zero. It means that all patients who have declared recovered should be managed to join in group S and no one is entered in group L or I.

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