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MATHEMATICAL MODELLING OF PRIMARY INFECTION TUBERCULOSIS WITH ASTHMA AS A SECOND INFECTION

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ABSTRACT

Tuberculosis is an infectious disease caused by Mycobacterium Tuberculosis. Tuberculosis patients undergoing long-term tuberculosis treatment have a high risk to get asthma as a second infection. A person suffering from asthma cannot recover. Asthma therapy is only to control the development of asthma so that asthma does not get worse. In this study we discusses the spread of tuberculosis with asthma as a secondary infection. We perform the model into system of non-linear differential equation that consist of six equation because the population divided into six sub-population which are susceptible, infected by tuberculosis, undergoing tuberculosis treatment, infected by asthma, undergoing asthma treatment and recovered from tuberculosis. From the model that has been formed, we perform the analysis to obtain the equilibrium point and the basic reproduction number. Then we show the local stability of the equilibrium point and perform simulations to provide an illustration. From the analytical result, we got that the spread influence by recruitment rate, infection rate, natural death rate, tuberculosis treatment rate and death rate because of tuberculosis.

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1. INTRODUCTION

Tuberculosis infects more than 9 million people and causes the death of 1.5 million people every year worldwide. Treatment of tuberculosis takes at least 6 months, causing drug resistance worldwide to increase and threaten the effectiveness of tuberculosis treatment [1]. Tuberculosis is a respiratory disease associated with asthma. Asthma become a common infection in patients with a history of tuberculosis who was successfully treated in the past [2], [3]. Asthma is a disease caused by inflammation of the bronchi which causes the bronchi to narrow, so that air flow in the bronchi to the lungs is limited [4]. Current asthma treatment including long-term control care and environmental control measures can reduce asthma exacerbations due to airborne allergens [5], [6].

Some mathematical modelling on tuberculosis has been done such as in [7] which purposes optimal control strategies to reduce the number of tuberculosis patient in Philippines. Another researchers in [8] purpose mathematical model which include diagnosis and treatment on their model. Mathematical modelling on asthma currently not an epidemiological models because asthma is not an infectious disease, such as in [9]. They present a computational model that describe mechanism in the lug.

Secondary infection mathematical model has been done by [10] but they were taking influenza as a primary infection and Bronchitis as a secondary infection. In their model, they gave treatment for influenzas but didn't put any treatment for the second infection. Based on this, we will do a mathematical modelling of the tuberculosis transmission with asthma as a secondary infection with each infection undergoing a different treatment. Next, an analysis of the equilibrium point and its local stability will be carried out on the mathematical model that has been formed. As a representation, a numerical simulation will be carried out using Maple software. Maple is a computer-based mathematical application for analytical and numerical mathematical calculations [11].

2. RESEARCH METHODS

To conduct this research first we collect the medical literature about tuberculosis and asthma. We also look up the mathematical model of secondary infection. Base on those literatures we build some assumption that proper to the medical phenomena then construct the mathematical models. After the mathematical models formed, we analyse the equilibrium points, the basic reproduction number, and their local stability. Finally, we do some simulation by choosing some parameters values. Some are based on data, but the others are by assumption. We describe the methods on Figure 1.

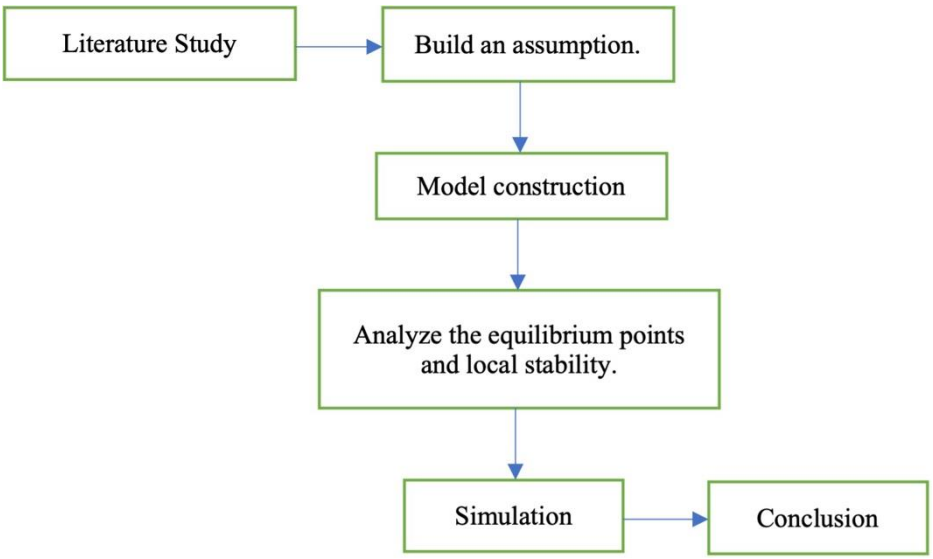


Figure 2. Research methods

3. RESULTS AND DISCUSSION

3.1 Mathematical Model

An infectious disease in a population will divide the population into several classes [11]. Mathematical modelling in this study was divided into 6 classes, which are healthy individuals are susceptible to tuberculosis infection (S), individuals infected with tuberculosis (I_1), individuals infected with tuberculosis undergoing treatment (T_1), individuals infected with asthma (I_2), individuals infected with asthma undergoing treatment (T_2), and individuals recovering from tuberculosis infection (R). The parameters used in the model are presented in the following Table 1.

Table 1. List of Parameter

Symbol	Definition	Condition
Λ	Recruitment rate	$\Lambda > 0$
β	Tuberculosis infection rate	$\beta > 0$
γ_1	Rate of tuberculosis patient into treatment	$\gamma_1 > 0$
γ_2	Rate of asthma patient into asthma treatment	$\gamma_2 > 0$
d_1	Dead rate of tuberculosis infected individuals	$d_1 > 0$
d_2	Dead rate of asthma infected individuals	$d_2 > 0$
σ	Rate of recovered tuberculosis patient	$0 < \sigma < 1$
μ	Natural dead rate	$\mu > 0$

The transmission model for tuberculosis disease with asthma as a secondary infection is illustrated in the modelling diagram is show in Figure 2 below

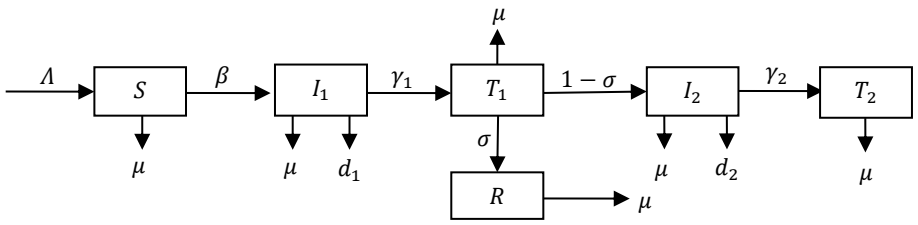


Figure 2. Transfer Diagram

The equation of the mathematical model is obtained as follows

$$\begin{aligned} S' &= \Lambda - \beta S I_1 - \mu S \\ I_1' &= \beta S I_1 - \gamma_1 I_1 - \mu I_1 - d_1 I_1 \\ T_1' &= \gamma_1 I_1 - \sigma T_1 - (1-\sigma) T_1 - \mu T_1 \\ I_2' &= (1-\sigma) T_1 - \gamma_2 I_2 - \mu I_2 - d_2 I_2 \\ T_2' &= \gamma_2 I_2 - \mu T_2 \\ R' &= \sigma T_1 - \mu R \end{aligned} \quad (1)$$

Through Equation (1), the equilibrium point can be found by making zeros on the right side of the equation. As a result, two equilibrium points are obtained, namely

1. Disease-free equilibrium point $(E_0) = (S^*, I_1^*, T_1^*, I_2^*, T_2^*, R^*) = \left(\frac{\Lambda}{\mu}, 0,0,0,0,0\right)$.
2. Endemic equilibrium point $(E_1) = (S^{**}, I_1^{**}, T_1^{**}, I_2^{**}, T_2^{**}, R^{**})$ with

$$S^{**} = \frac{\gamma_1 + \mu + d_1}{\beta}$$

$$I_1^{**} = \frac{\Lambda\beta - \mu(\gamma_1 + \mu + d_1)}{\beta(\gamma_1 + \mu + d_1)}$$

$$T_1^{**} = \frac{\gamma_1\left(\Lambda\beta - \mu(\gamma_1 + \mu + d_1)\right)}{\beta(1+\mu)(\gamma_1 + \mu + d_1)}$$

$$I_2^{**} = \frac{\gamma_1(1-\sigma)\left(\Lambda\beta - \mu(\gamma_1 + \mu + d_1)\right)}{\beta(1+\mu)(\gamma_1 + \mu + d_1)(\gamma_2 + \mu + d_2)}$$

$$T_2^{**} = \frac{\gamma_1\gamma_2(1-\sigma)\left(\Lambda\beta - \mu(\gamma_1 + \mu + d_1)\right)}{\mu\beta(1+\mu)(\gamma_1 + \mu + d_1)(\gamma_2 + \mu + d_2)}$$

$$R^{**} = \frac{\sigma\gamma_1\left(\Lambda\beta - \mu(\gamma_1 + \mu + d_1)\right)}{\beta\mu(\sigma + \mu)(\gamma_1 + \mu + d_1)}$$

The development of transmission of tuberculosis disease with asthma as a secondary infection is determined by the basic reproduction number (R_0) by finding the largest positive eigen values with the next generation matrix involving compartments that cause infection **[12],** namely $I_1, T_1, I_2,$ and T_2. By some computation obtained the value of $R_0 = \frac{\Lambda\beta}{\mu(\gamma_1+\mu+d_1)}$. The existence of the equilibrium points given in **Theorem 1** as follows.

Theorem 1. Given $R_0 = \frac{\Lambda\beta}{\mu(\gamma_1+\mu+d_1)}$.

1. If $R_0 \leq 1$, then the system of **Equation (1)** has one equilibrium point, which is the disease-free equilibrium point (E_0).
2. If $R_0 > 1$, then the system of **Equation (1)** has two equilibrium points, which are the disease-free equilibrium point (E_0) and the endemic equilibrium point (E_1).

Proof. To find the equilibrium we solve the system equal to zero, so we will have

$$\begin{aligned}
&\Lambda - \beta S I_1 - \mu S = 0\\
&\beta S I_1 - \gamma_1 I_1 - \mu I_1 - d_1 I_1 = 0\\
&\gamma_1 I_1 - \sigma T_1 - (1-\sigma) T_1 - \mu T_1 = 0\\
&(1-\sigma) T_1 - \gamma_2 I_2 - \mu I_2 - d_2 I_2 = 0\\
&\gamma_2 I_2 - \mu T_2 = 0\\
&\sigma T_1 - \mu R = 0
\end{aligned}$$

From the second equation we got

$$\beta S I_1 - \gamma_1 I_1 - \mu I_1 - d_1 I_1 = 0 \Leftrightarrow (\beta S - \gamma_1 - \mu - d_1) I_1 = 0$$

And we can conclude that

$$I_1 = 0 \quad \text{or } \beta S - \gamma_1 - \mu - d_1 = 0$$

While $I_1 = 0$ it is easy to substitute and get the free disease equilibrium point

$$E_0 = (S^*, I_1^*, T_1^*, I_2^*, T_2^*, R^*) = \left(\frac{\Lambda}{\mu}, 0,0,0,0,0\right).$$

While $\beta S - \gamma_1 - \mu - d_1 = 0$, then $S = \frac{\gamma_1+\mu+d_1}{\beta}$. Substituting this S into system (1) then we will get the second equilibrium point

$$E_1 = (S^{**}, I_1^{**}, T_1^{**}, I_2^{**}, T_2^{**}, R^{**})$$

as mentioned above. But we need a positive equilibrium point, and by define $R_0 = \frac{\Lambda\beta}{\mu(\gamma_1+\mu+d_1)}$ the existence of the second equilibrium point will be guaranteed while $R_0 > 1$.■

Then stability analysis will be carried out using the linearization method. So that the eigen values of the Jacobian matrix are obtained. The Jacobian matrix is as follows.

$$J(E) = \begin{pmatrix}
-\beta I_1 - \mu & -\beta S & 0 & 0 & 0 & 0\\
\beta I_1 & \beta S - \gamma_1 - \mu - d_1 & 0 & 0 & 0 & 0\\
0 & \gamma_1 & -\mu - 1 & 0 & 0 & 0\\
0 & 0 & 1-\sigma & -\mu - \gamma_2 - d_2 & 0 & 0\\
0 & 0 & 0 & \gamma_2 & -\mu & 0\\
0 & 0 & \sigma & 0 & 0 & -\mu
\end{pmatrix}$$

Next, substitute the value of the equilibrium point into the Jacobian matrix and look for the eigen values from matrix $J(E)$ using the formula $det(\lambda I - J(E)) = 0$. Equality this called equality characteristics from $J(E)$ **[13], [14] , [8], [9]**. The results were analyzed using the Routh-Hurwitz criteria. **Theorem 2** was obtained as follows.

Theorem 2. Given R_0 by the system of **Equation (1)**. Based on R_0 this obtained

1. The disease-free equilibrium point is (E_0) locally asymptotically stable if $R_0 < 1$.

2. The endemic equilibrium point is (E_1) locally asymptotically stable if $R_0 > 1$.

Proof. Substitute E_0 to the Jacobian we got characteristic equation as follow:

$$(\lambda+\mu)(\lambda+\mu)(\lambda+\mu+\gamma_2+d_2)(\lambda+\mu)\big(\lambda-(\beta S^*-\gamma_1-\mu-d_1)\big)(\lambda+\mu+1)=0.$$

So that we will have six eigen value which are

$\lambda_1 = -\mu$
$\lambda_2 = -\mu$
$\lambda_3 = -(\mu+\gamma_2+d_2)$
$\lambda_4 = -\mu$
$\lambda_5 = \beta S^* - \gamma_1 - \mu - d_1$
$\lambda_6 = -(\mu+1).$

Because all parameters are non-negative we only need to check λ_5. From the previous result, we got $S^* = \frac{R_0(\gamma_1+\mu+d_1)}{\beta}$, and substitute it to λ_5, we will have

$$\begin{aligned}\lambda_5 &= \beta S^* - \gamma_1 - \mu - d_1\\ &= \beta\left(\frac{R_0(\gamma_1+\mu+d_1)}{\beta}\right) - \gamma_1 - \mu - d_1\\ &= R_0(\gamma_1+\mu+d_1) - \gamma_1 - \mu - d_1\\ &= R_0(\gamma_1+\mu+d_1) - (\gamma_1+\mu+d_1)\\ &= (\gamma_1+\mu+d_1)(R_0-1).\end{aligned}$$

Here we can conclude that if $R_0 < 1$ then all of the eigen values are negative, or in other word E_0 is locally asymptotically stable.

Substitute E_1 to the Jacobian we got the characteristic equation as follow:

$$(\lambda+\mu)(\lambda+\mu)(\lambda+\mu+\gamma_2+d_2)\Big[(\lambda+\mu(R_0-1)+\mu)(\lambda)(\lambda+\mu+1) - \Big((-(\gamma_1+\mu+d_1))\big(\mu(R_0-1)\big)(\lambda+\mu+1)\Big)\Big]=0$$

Then the eigen values are
$\lambda_1 = -\mu$
$\lambda_2 = -\mu$
$\lambda_3 = -(\mu+\gamma_2)$

and λ_4, λ_5, dan $\lambda_6$are solutions of

$$(\lambda+\mu(R_0-1)+\mu)(\lambda)(\lambda+\mu+1) - \Big((-(\gamma_1+\mu+d_1))\big(\mu(R_0-1)\big)(\lambda+\mu+1)\Big)=0.$$

Using Ruth-Hurwitz criterion can be seen that if $R_0 > 1$ then all real part of the eigen values are negative, or in other word E_1 is locally asymptotically stable.■

3.2 Numerical Simulations

Then the model is simulated using the initial values $S(0)=2$, $I_1(0)=1$, $T_1(0)=0$, $I_2(0)=0$, $T_2(0)=0$, and $R(0)=0$. The parameter values stated are as in **Table 2** below

Table 2. Parameter Value

Parameter	Values	Source
Λ	0.45	[15]
β	0.5	[16]
γ_1	0.3	[15]
γ_2	0.9767	[17]
d_1	0.022722	[15]
d_2	0.001737	[18]
σ	0.304	[2]
μ	0.3	[19]

3.2.1 Simulation around the Disease-Free Equilibrium Point(E_0)

The parameter value is γ_1 enlarged to 0.5 then the basic reproduction number is obtained $R_0 =$ 0,9116080523. Because $R_0 < 1$ then there is a disease-free condition. Obtained value $E_0 = (S^*, I_1^*, T_1^*, I_2^*, T_2^*, R^*) =$ (1.5, 0, 0, 0, 0, 0). The graph is shown in **Figure 2** below

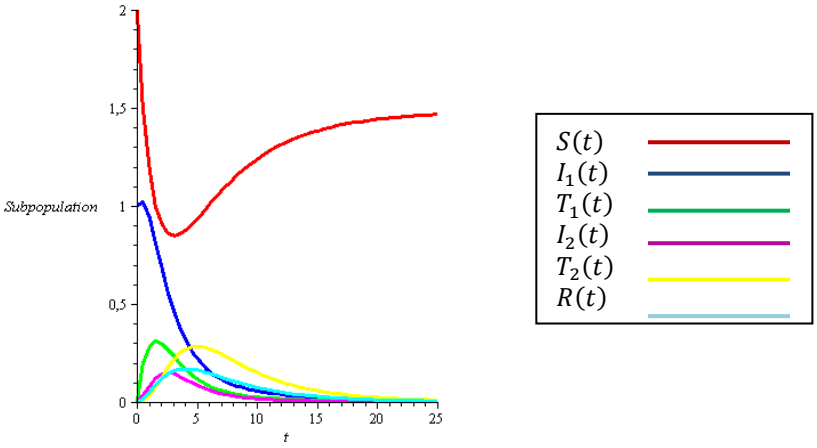


Figure 2. Simulation of Disease-Free Equilibrium Point

Based on **Figure 2** above, it can be seen that healthy individuals who are susceptible to tuberculosis (S) have decreased in their initial conditions. Then the size of susceptible individuals increases to a certain t and there is no change or constant at a point 1,5 at a certain t. As for the other populations, individuals infected with tuberculosis (I_1), individuals infected with tuberculosis underwent treatment for tuberculosis (T_1), individuals infected with asthma (I_2), individuals infected with asthma underwent treatment for asthma (T_2), and individuals recovered from tuberculosis (R) experienced an increase over time t. Then it decreases until a time t and is constant at zero.

3.2.2 Simulation Analysis at the Endemic Equilibrium Point(E_1)

While we set parameter value $\gamma_1 = 0{,}3$ then obtained the basic reproduction number $R_0 =$ 1,20438976. Because $R_0 > 1$there will be endemic conditions. Obtained values $E_0 = (S^{**}, I_1^{**}, T_1^{**}, I_2^{**}, T_2^{**}, R^{**}) =$ (1.245444, 0.122633866, 0.02830012062, 0.01540700398, 0.05016006932, 0.02867745556). The graph is shown in **Figure 3** below

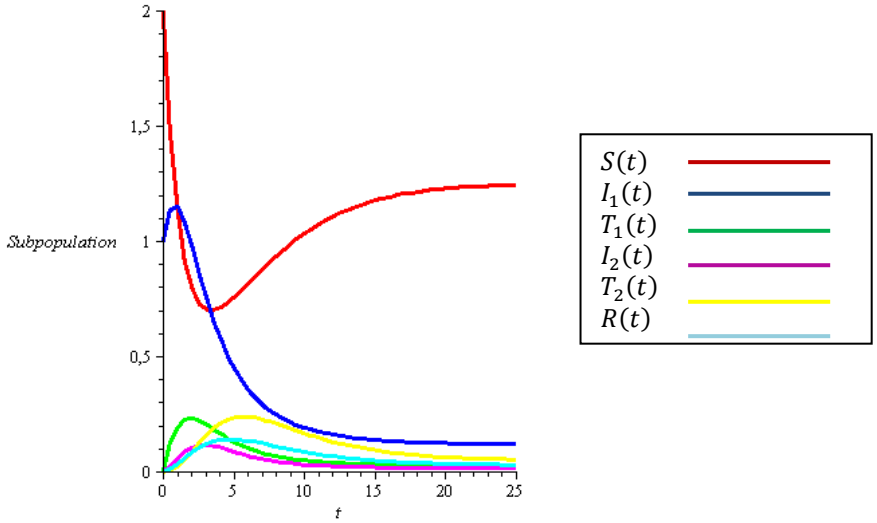


Figure 3. Endemic Equilibrium Point Simulation

Based on **Figure 3** above, it is found that healthy individuals who are susceptible to tuberculosis infection $S(t)$ have decreased in their initial conditions. Then the size of susceptible individuals increases to a certain t and there is no change or constant at a point 1.245444 at a certain t.Individuals infected with tuberculosis $I_1(t)$ experienced an increase in initial conditions. Then up to a certain point when the tindividual infected with tuberculosis decreased and there was no change or constant at the point 0.12263 at a certain

t.Individuals infected with tuberculosis who underwent tuberculosis treatment $T_1(t)$ experienced an increase in baseline conditions. Then up to a certain point when tindividuals infected with tuberculosis undergoing treatment experience a decrease and there is no change or constant at a the point 0.02830 at a certain t.Individuals infected with asthma $I_2(t)$ have an increase in initial conditions. Then up to a certain point when tan individual is infected with asthma there is a decrease and there is no change or constant at the point 0.01541 at a certain t.Individuals infected with asthma undergoing asthma treatment $T_2(t)$ experienced an increase in initial conditions. Then up to a certain point when tan individual is infected with tuberculosis, there is a decrease and there is no change or constant at the point of 0.05106 at a certain t.Individuals recovering from tuberculosis $R(t)$ experienced an increase in initial conditions. Then up to a certain point when the tindividual recovers from tuberculosis, there is a decrease and there is no change or constant at the point 0.02868 at a certain t.

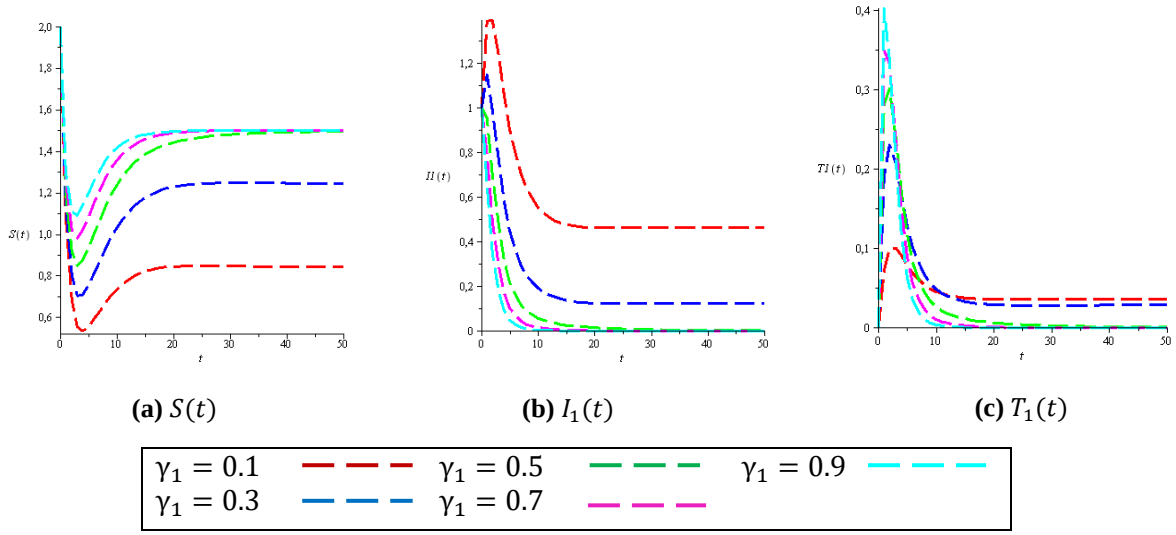
3.2.3 Changing on Parameter Value γ_1

To determine the effect of tuberculosis treatment rate, we varying the value of the parameters $\gamma_1$presented in **Table 3** below:

Table 3. Variation of Parameters γ_1 at The Equilibrium Point

γ_1	R_0	Equilibrium point$(S, I_1, T_1, I_2, T_2, R)$
0.1	1.774215678	(0.84544, 0.46453, 0.03573, 0.01945, 0.06333, 0.03621)
0.3	1.204389760	(1.24544, 0.12263, 0.02830, 0.01541, 0.05016, 0.02868)
0.5	0.9116080523	(1.5, 0, 0, 0, 0, 0)
0.7	0.7333371141	(1.5, 0, 0, 0, 0, 0)
0.9	0.6133855447	(1.5, 0, 0, 0, 0, 0)

Obtained a graph as shown in **Figure 4** below.



(a) $S(t)$ **(b)** $I_1(t)$ **(c)** $T_1(t)$

Figure 4. Simulation of the effect of tuberculosis treatment rate for each sub-population, (a) susceptible sub-population, (b) tuberculosis patients sub-population, (c) tuberculosis patients undergoing treatment sub-population.

Based on **Figure 4** (a), and **Figure 4** (b) it can be seen that the lower the rate of tuberculosis treatment, the higher the number of individuals in the $S(t)$ and $I_1(t)$. While in **Figure 4** (c) it can be seen that the lower the rate of tuberculosis treatment, the lower the number of individuals in the sub-population $T_1(t)$. The sub-population $I_2(t)$, $T_2(t)$, and $R(t)$ has the same graph as in **Figure 4** (c). It can be seen that the lower the rate of tuberculosis treatment results in the lower number of individuals infected with asthma, asthma-infected individuals undergoing asthma treatment, and individuals recovering from tuberculosis. The effect of tuberculosis treatment rate on individuals in each population is the higher the effect of tuberculosis treatment, the faster the development of individuals in each population will reach a stable point in time t increased rate of tuberculosis treatment.

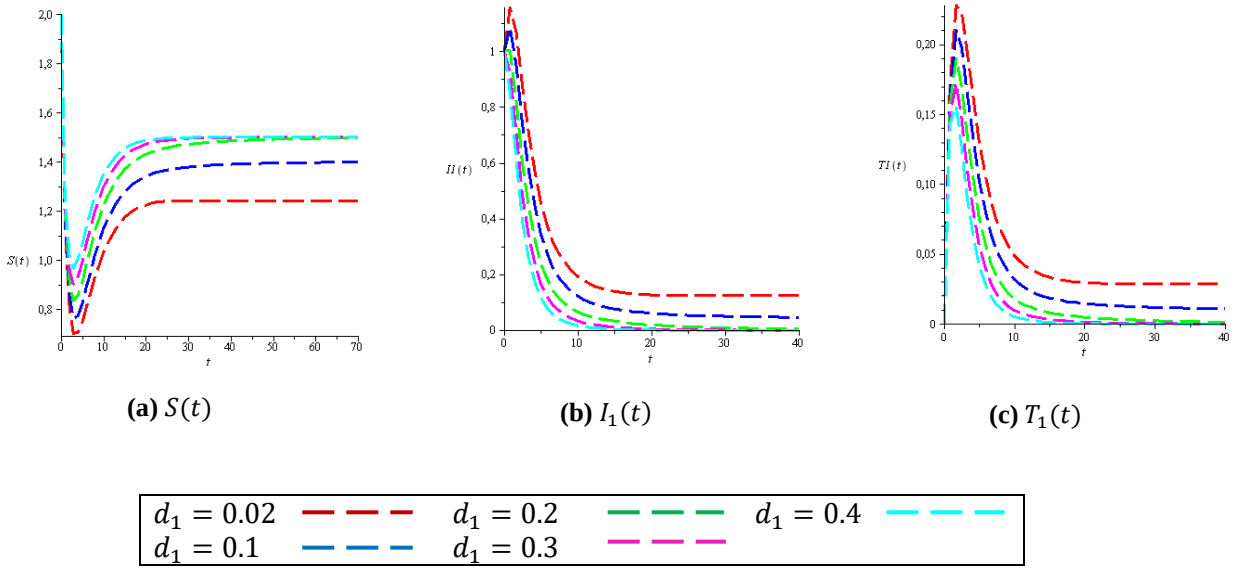
3.2.4 Changing on Parameter Value d_1

To find out the effect of the death rate of an individual infected with tuberculosis, it will be done by varying the value of the parameter value d_1 presented in **Table 4** below:

Table 4. Parameter Variations d_1 at The Equilibrium Point

d_1	R_0	Equilibrium point$(S, I_1, T_1, I_2, T_2, R)$
0.02	1.209677419	(1.24000, 0.12581, 0.02903, 0.01581, 0.05146, 0.02942)
0.1	1.071428571	(1.40000, 0.04286, 0.00989, 0.00538, 0.01753, 0.01002)
0.2	0.937500000	(1.5, 0, 0, 0, 0, 0)
0.3	0.833333333	(1.5, 0, 0, 0, 0, 0)
0.4	0.750000000	(1.5, 0, 0, 0, 0, 0)

Obtained a graph as shown in **Figure 5** below



(a) $S(t)$ **(b)** $I_1(t)$ **(c)** $T_1(t)$

Figure 5. Simulation by Varying the Death Ratescaused of Tuberculosis on (a)susceptible sub-population, (b)tuberculosis patients sub-population, (c)tuberculosis patients undergoing treatment sub-population.

Based on **Figure 5** (a), **Figure 5** (b), and **Figure 5** (c) it can be seen that the lower the death rate of individuals infected with tuberculosis, the higher the number of individuals in each population. Population $I_2(t)$, $T_2(t)$, and $R(t)$ have the same graph as in **Figure 5** (c). It can be seen that the lower the death rate of individuals infected with tuberculosis, the higher the number of individuals infected with asthma, asthma-infected individuals undergoing asthma treatment, and individuals recovering from tuberculosis. The effect of the death of an individual infected with tuberculosis on an individual in each population is the higher the effect of the death of an individual infected with tuberculosis, the faster the development of individuals in each population will reach a stable point in time t. So, to achieve a disease-free condition or a condition where tuberculosis disease with asthma as a secondary infection will disappear, it is necessary to increase the proportion of deaths of individuals infected with tuberculosis.

4. CONCLUSIONS

Through this research, it is found that the mathematical model of the spread of tuberculosis with asthma as a secondary infection has two equilibrium points, which are the disease-free equilibrium point (E_0) and the endemic equilibrium point (E_1). The spread of tuberculosis with asthma as a secondary infection is indicated by the basic reproduction number (R_0) that influenced by recruitment rate, infection rate, the natural death rate, tuberculosis treatment rate and the death rate of tuberculosis patient. The disease-free equilibrium point is (E_0) locally asymptotically stable if $R_0 < 1$. Meanwhile, the endemic equilibrium point is (E_1) locally asymptotically stable if $R_0 > 1$. Based on the numerical simulations performed, it was found that the change in the proportion value γ_1 had d_1 a significant effect on the basic reproduction value (R_0)

and the equilibrium point obtained. By giving a value γ_1 and d_1 the higher it will decrease the value R_0 and the development of individuals in each population is getting faster towards a stable point.

REFERENCES

[1] C. R. Hosburgh, C. E. Barry, and C. Lange, "Treatment of Tuberculosis," *New england journal of medicine*, vol. 22, no. 373, pp. 2149–2160, 2015.

[2] K. Garg and J. K. Karahyla, "Association between tuberculosis and bronchial asthma," *International Journal of Research in Medical Sciences*, vol. 5, no. 8, pp. 3566–3569, 2017.

[3] F. Maula, A. Suleman, M. Yasin, and M. Zaman, "Frequency of Bronchial Asthma in Post-Tuberculosis Patients," *Pakistan Journal of Chest Medicine*, vol. 20, no. 3, pp. 86–88, 2014.

[4] M. Schatz and L. Rosenwasser, "The Allergic Asthma Phenotype," *Journal of Allergy and Clinical Immunology: In Practice*, vol. 2, no. 6, pp. 645–648, 2014.

[5] J. Alwarith *et al.*, "The role of nutrition in asthma prevention and treatment," *Nutrition Reviews*, vol. 78, no. 11, pp. 928–938, 2020.

[6] A. Litanto and K. Kartini, "Kekambuhan asma pada perempuan dan berbagai faktor yang memengaruhinya: sebuah tinjauan," *Jurnal Biomedika dan Kesehatan*, vol. 4, no. 2, pp. 79–86, 2021.

[7] S. Kim, A. A. D. L. R. V, and E. Jung, "Mathematical model and intervention strategies for mitigating tuberculosis in the Philippines," *Journal of Theoretical Biology*, vol. 443, pp. 100–112, 2018.

[8] A. O. Egonmwan and D. Okuonghae, "Analysis of a mathematical model for tuberculosis with diagnosis," *Journal of Applied Mathematics and Computing*, vol. 59, pp. 129–162, 2018.

[9] T. Winkler, J. G. Venegas, and R. S. Harris, "Computational models of lung diseases Mathematical modeling of ventilation defects in asthma," *Drug Discovery Today: Disease Models*, vol. 15, pp. 3–8, 2015.

[10] V. K. Bais and D. Kumar, "Mathematical Analysis on Bronchitis Infection," *IEEE Xplore*, pp. 1861–1864, 2016.

[11] W. Gander, M. J. Gander, and F. Kwok, *Scientific Computing An Introduction using Maple and MATLAB*. Switzerland: Springer, 2014.

[12] P. Van Den Driessche, "Reproduction Numbers of Infectious Disease Models," *Infectious Disease Modelling*, pp. 1–29, 2017.

[13] H. Anton and C. Rosses, *Elementary Linear Algebra*, 11 th. Canada: Wiley, 2014.

[14] R. Mahardika, Widowati, and Y. Sumanto, "Routh-hurwitz criterion and bifurcation method for stability analysis of tuberculosis transmission model," *Journal of Physics*, 2019.

[15] S. Side, W. Sanusi, and N. F. Setiawan, "Analisis dan Simulasi Model SITR pada Penyebaran Penyakit Tuberkulosis di Kota Makassar," *Jurnal Sainsmat*, vol. 5, no. 2, pp. 191–204, 2016.

[16] R. W. Tanjung, Muhafzan, and Zulakmal, "Model Penyebaran Penaykit Tuberkulosis dengan Kontrol Vaksinasi," *Jurnal Matematika UNAND*, vol. 10, no. 3, pp. 280–287, 2021.

[17] A. Lorensia and A. D. Pratiwi, "Analisis permasalahan terkait obat pada pengobatan pasien asma rawat inap," *Farmasains*, vol. 8, no. 2, pp. 87–96, 2021.

[18] WHO, "Asthma," 2022. https://www.who.int/news-room/fact-sheet/detail/asthma (accessed Aug. 03, 2022).

[19] I. A. Baba, R. A. Abdulkadir, and P. Esmaili, "Analysis of tuberculosis model with saturated incidence rate and optimal control," *Physica A*, p. 123237, 2019.