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Research Article

Global Stability of SIR and SEIR Model for Tuberculosis Disease Transmission with Lyapunov Function Method

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Abstract

Background and Objective: Tuberculosis (TB) is an infectious disease that poses a threat to the human population in the world. The aimed of study discussed are to build a model SIR and SEIR tuberculosis disease transmission and analysis for both models. **Methodology:** The SIR model is a system of ordinary differential equations four dimension and SEIR model is a system of ordinary differential equations five dimension. Both models are then analyzed by building a mathematical theorem, which guarantees the existence of a case of TB, the disease-free equilibrium phase and stage of disease endemic TB. **Results:** Three theorems proving using the Lyapunov function method. Basic reproduction number R_0 also be obtained from the two models, namely, if $R_0 > 1$ then obtained asymptotically stable equilibrium endemic globally and if the basic reproduction number $R_0 \leq 1$, acquired the disease-free equilibrium global asymptotically stable. **Conclusion:** The results of both models can be used to determine the status of TB disease in a region by conducting a simulation using data in the region.

Key words: TB disease, SIR and SEIR model, Lyapunov function, global stability, free disease, endemic

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

World Health Organization (WHO)¹ states that in 1995, 0.33 of the world population has been infected tuberculosis (TB), 9 million new patients and 3 million deaths worldwide, 95% of TB cases and 98% of deaths worldwide occur in developing countries.

The TB infection can be divided into two kinds, namely, latently infected and actively infected. Latent infected is a condition, in which the patient's body found in TB bacteria that are dormant (sleeping), does not cause TB disease in the patient's body, but in a certain period of time that are dormant bacteria was able to get up and be active. People who are infected with latent called latent TB patients. A person with latent TB is not spread by TB bacteria to people who are vulnerable to TB disease. Actively infected is a condition in which the patient's body to be active TB bacteria breed and cause symptoms of TB disease. Actively infected person is called active TB patients. People with active TB disease can transmit TB to people who are susceptible to tuberculosis².

People with latent TB and active TB patients can be cured, but they are not immune or resistant. Within a certain period of tuberculosis patients who had recovered can be re-infected TB. The events of the infection by tuberculosis bacteria can be described that in a population is divided into subpopulations. Namely subpopulations are susceptible that are vulnerable to TB disease, infectious latent is a population of patients with latent tuberculosis, active infectious is a infected TB disease and recovered patients are cured of latent tuberculosis².

Mathematical models have found several study propose compartmental dynamics such as Susceptible, Infected and Recovered (SIR) models³⁻⁸ and Susceptible, Exposed, Infected and Recovered (SEIR) models⁹⁻¹⁴.

In this study, analysis of the global stability for the models SIR and SEIR will be studied by Lyapunov function method. This method is a powerful technique for multidimensional system for establishing conditions for global dynamics of the four dimensional SIR model and the five dimensional SEIR model of TB disease. Both models are resolved through the use of Lyapunov functions adopted from Tewa *et al.*¹⁵ and Syafruddin and Noorani¹⁶. In particular, this study follows closely the ideas used recently by Syafruddin and Noorani¹⁶ to establish the global stability of the endemic equilibrium.

MATERIALS AND METHODS

SIR model formulation for TB: Changes that occur in every human population on the transmission of TB disease SIR model adopted by Side¹⁷ can be interpreted in the form of Fig. 1.

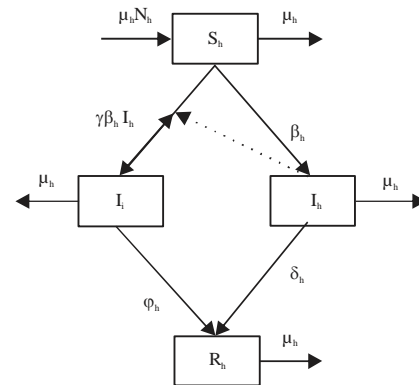


Fig. 1: Human population for TB transmission SIR model

The rate of change in the number of people who easily infected with respect to time is $\left(\frac{dS_h}{dt}\right)$ affected by the number of births that is $\mu_h N_h$, a human population reduced the number of people infected by the virus directly $\gamma \beta_h I_h S_h$, the number of people infected by the virus from infected humans are healthy $\beta_h S_h$ and the number of people who die $\mu_h S_h$ can be interpreted as follows in Eq. 1:

$$\frac{dS_h}{dt} = \mu_h N_h - \beta_h S_h - \gamma \beta_h I_h S_h - \mu_h S_h \tag{1}$$

The rate of change in the number of people infected with respect to time is $\left(\frac{dI_h}{dt}\right)$ influenced by the amount of human population has been infected because the virus directly reduced the number of deaths of infected human population $\mu_h I_h$ and the number of human populations to recover from an outbreak $\delta_h I_h$ can be interpreted as follows in Eq. 2:

$$\frac{dI_h}{dt} = \beta_h S_h - (\mu_h + \delta_h) I_h \tag{2}$$

The rate of change in the number of people infected with respect to time is $\left(\frac{dI_i}{dt}\right)$ influenced by the amount of human population has been infected because as human virus infected human population reduced the number of deaths $\mu_h I_i$ and the number of infected human populations recovered from outbreaks $\phi_h I_i$ can be interpreted in Eq. 3 as follows:

$$\frac{dI_i}{dt} = \gamma \beta_h I_h S_h - (\mu_h + \phi_h) I_i \tag{3}$$

The rate of change in the number of human populations recover over time $\left(\frac{dR_h}{dt}\right)$ is the difference rather than the number of people who have recovered from the infection $\delta_h I_h$ and $\mu_h I_i$ dengan jumlah kematian manusia pulih $\mu_h R_h$, the number of human deaths recovered can be interpreted in Eq. 4 as follows:

$$\frac{dR_h}{dt} = \delta_h I_h + \varphi_h I_i - \mu_h R_h \quad (4)$$

Figure 1 can also be interpreted in the form of a mathematical model that the model is not linear differential Eq. 5 as follows:

$$\frac{dS_h}{dt} = \mu_h N_h - \beta_h S_h - \gamma \beta_h I_h S_h - \mu_h S_h \quad (5)$$

$$\frac{dI_h}{dt} = \beta_h S_h - (\mu_h + \delta_h) I_h$$

$$\frac{dI_i}{dt} = \gamma \beta_h I_h S_h - (\mu_h + \varphi_h) I_i$$

$$\frac{dR_h}{dt} = \delta_h I_h + \varphi_h I_i - \mu_h R_h$$

With $N_h(t) = S_h(t) + I_h(t) + I_i(t) + R_h(t)$ or:

$$R_h(t) = N_h(t) - (S_h(t) + I_h(t) + I_i(t))$$

The system of Eq. 5 is not linear differential equations to model SIR of TB. The resulting model can be simplified by assuming the following fractions:

$$x(t) = \frac{S_h}{N_h}, \quad y(t) = \frac{I_h}{N_h} \quad \text{and} \quad z(t) = \frac{I_i}{N_h}$$

So the human population model for the transmission of TB disease can be simplified as shown in Eq. 6:

$$\frac{dx}{dt} = \mu_h - \beta_h x - \gamma \beta_h xy - \mu_h x \quad (6)$$

$$\frac{dy}{dt} = \beta_h x - \alpha y$$

$$\frac{dz}{dt} = \gamma \beta_h xy - \eta z$$

With $\alpha = \mu_h + \delta_h$ dan $\eta = \mu_h + \varphi_h$.

SEIR model formulation for TB: Changes that occur in every human population on the transmission of TB disease for SIR model can be interpreted in the form of Fig. 2.

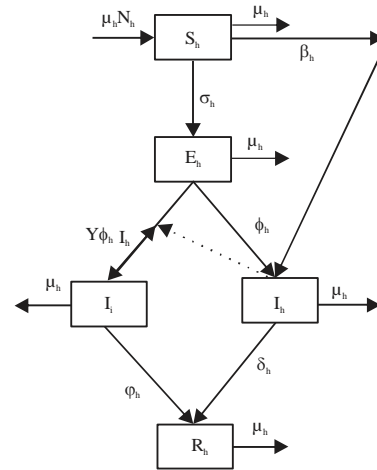


Fig. 2: Human population for TB transmission with SEIR model

The rate of change in the number of people who easily infected with respect to time is $\left(\frac{dS_h}{dt}\right)$ affected by the number of births human population is $\mu_h N_h$ reduced the number of people infected by the virus directly $\beta_h S_h$, the number of people showing symptoms of infection $\sigma_h S_h$ and the number of healthy human beings who die $\mu_h S_h$ can be interpreted in Eq. 7 as follows:

$$\frac{dS_h}{dt} = \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h \quad (7)$$

The rate of change in the number of people who show symptoms of infection over time is $\left(\frac{dE_h}{dt}\right)$ affected by the number of people showing symptoms of infection $\sigma_h S_h$ reduced the human population has been infected because the virus directly $\phi_h E_h$, the number of human population has been infected because the virus from infected humans $\gamma \phi_h I_h E_h$ and the number of deaths of human populations $\mu_h E_h$ berikut can be interpreted in Eq. 8 as follows:

$$\frac{dE_h}{dt} = \sigma_h S_h - \gamma \phi_h I_h E_h - \phi_h E_h - \mu_h E_h \quad (8)$$

The rate of change in the number of people infected by the virus of the time $\left(\frac{dI_h}{dt}\right)$ is influenced by the amount of human population has been infected because the virus directly $\beta_h S_h$ and the number of people showing symptoms of infection (Exposed) $\phi_h E_h$ reduced the number of deaths of infected human population $\mu_h I_h$ and the number of human populations to recover from an outbreak $\delta_h I_h$ can be interpreted in Eq. 9 as follows:

$$\frac{dI_h}{dt} = \beta_h S_h + \phi_h E_h - (\mu_h + \delta_h) I_h \quad (9)$$

The rate of change in the number of people infected by the virus from infected humans is $\left(\frac{dI_i}{dt}\right)$ influenced by the human population has been infected because the virus infected humans reduced the number of deaths of infected human population $\mu_h I_h$ and the number of human populations to recover from an outbreak $\phi_h I_h$ can be interpreted as follows in Eq. 10:

$$\frac{dI_i}{dt} = \gamma \phi_h I_h E_h - (\mu_h + \phi_h) I_i \quad (10)$$

The rate of change in the number of human populations recover over time $\left(\frac{dR_h}{dt}\right)$ is the difference of the number of people who have recovered from the infection $\delta_h I_h$ and $\mu_h I_i$ the number of human deaths recovered $\mu_h R_h$ can be interpreted in Eq. 11 as follows:

$$\frac{dR_h}{dt} = \delta_h I_h + \mu_h I_i - \mu_h R_h \quad (11)$$

Figure 2 can also be interpreted in the form of a mathematical model that the model is not linear differential Eq. 12 as follows:

$$\frac{dS_h}{dt} = \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h \quad (12)$$

$$\frac{dE_h}{dt} = \sigma_h S_h - \gamma \phi_h I_h E_h - \phi_h E_h - \mu_h E_h$$

$$\frac{dI_h}{dt} = \beta_h S_h + \phi_h E_h - (\mu_h + \delta_h) I_h$$

$$\frac{dI_i}{dt} = \gamma \phi_h I_h E_h - (\mu_h + \phi_h) I_i$$

$$\frac{dR_h}{dt} = \delta_h I_h + \mu_h I_i - \mu_h R_h$$

With $N_h(t) = S_h(t) + E_h(t) + I_h(t) + I_i(t) + R_h(t)$ or:

$$R_h(t) = N_h(t) - (S_h(t) + E_h(t) + I_h(t) + I_i(t))$$

The system of Eq. 12 is not linear differential equations to model the SIR of TB disease. The resulting model can be simplified by assuming the following fractions:

$$x(t) = \frac{S_h}{N_h}, y(t) = \frac{I_h}{N_h}, z(t) = \frac{I_i}{N_h}, \text{ dan } u(t) = \frac{E_h}{N_h}$$

So the human population model for the transmission of TB disease can be simplified as shown in Eq. 12 following Eq. 13 and 14:

$$\frac{dx}{dt} = \mu_h - \beta_h x - \sigma_h x - \mu_h x \quad (13)$$

$$\frac{du}{dt} = \sigma_h x - \gamma \phi_h y u - \phi_h u - \mu_h u$$

$$\frac{dy}{dt} = \beta_h x + \phi_h u - \alpha y$$

$$\frac{dz}{dt} = \gamma \phi_h y u - \eta z$$

With:

$$\alpha = \mu_h + \delta_h \text{ dan } \eta = \mu_h + \phi_h \quad (14)$$

RESULTS AND DISCUSSION

Positivity of solutions for SIR model: Since the system 5 is dealing with population of TB, all the variables and parameters of the model are non-negative. It was claimed the following:

Theorem 1: Let $(S_h(t) > 0, I_h(t) > 0, I_i(t) > 0, R_h(t) > 0)$ the completion of the system 5 with the initial state $(S_{0h}, I_{0h}, I_{0i}, R_{0h})$ and compact set as in Eq. 15:

$$D = \{(S_h(t), I_h(t), I_i(t), R_h(t)) \in \mathbb{R}_+^4, L \leq N_h\} \quad (15)$$

To model the system 5, D is a positively invariant set that covers all settlement in \mathbb{R}_+^4 .

Proof: Consider the Lyapunov function candidate for the following:

$$L(t) = S_h + I_h + I_i + R_h$$

Derivative of the function with respect to time satisfied as in Eq. 16:

$$\begin{aligned} \left(\frac{dL}{dt}\right) &= S'_h + I'_h + I'_i + R'_h \\ &= \mu_h N_h - \beta_h S_h - \gamma \beta_h I_h S_h - \mu_h S_h + \beta_h S_h - \\ &\quad (\mu_h + \delta_h) I_h + \gamma \beta_h I_h S_h - (\mu_h + \phi_h) I_i \\ &\quad + \delta_h I_h + \phi_h I_i - \mu_h R_h \\ &= \mu_h N_h - \mu_h L(t) \end{aligned} \quad (16)$$

Not difficult to prove that in Eq. 17:

$$\frac{dL}{dt} = \mu_h N_h - \mu_h L(t) \leq 0 \text{ for } L \geq N_h \quad (17)$$

Then, from the above Eq. 17, it is known that $dL/dt \leq 0$ that means that D is a set of positive invariant. Conversely, by completing the system 16 is obtained that, $0 \leq L(t) \leq N_h + L(0)e^{-\mu_h t}$, which L(0) is the initial condition of L(t) in Eq. 18.

Therefore, if:

$$t \rightarrow \infty, 0 \leq L(t) \leq N_h \quad (18)$$

and concluded that D is a set of positive invariant and cover all of the settlement in R_+^5 . This proves the theorem.

This theorem guarantees the existence of TB disease in an area that was initially not found a virus carrier TB bacteria then changed after the discovery of the population suspected but not yet infected, $S_h(t) > 0$, infected with TB, $I_h(t) > 0$, TB infected by people who have a positive TB, $I_i(t) > 0$ and recovered human $R_h(t) > 0$ from bacteria TB. This theorem also gives the conclusion that further investigation of TB cases this stage so that we can identify the stage of disease spread TB to the endemic phase of SIR model.

Positivity of solutions for SEIR model: Since the system 12 is dealing with population of TB, all the variables and parameters of the model are non-negative. It was claimed the following:

Theorem 2: Let $(S_h(t) > 0, E_h(t) > 0, I_h(t) > 0, I_i > 0, R_h(t) > 0)$ completion of the system 12 with the initial state $(S_{0h}, E_{0h}, I_{0h}, I_{0i}, R_{0h})$ and compact set in Eq. 19:

$$D = \left\{ (S_h(t), E_h(t), I_h(t), I_i(t), R_h(t) \in R_+^5, L \leq N_h) \right\} \quad (19)$$

To model the system 12, D is a positively invariant set that covers all settlement in R_+^5 .

Proof: Consider the Lyapunov function candidate for the following:

$$L(t) = S_h + E_h + I_h + I_i + R_h$$

Derivative of the function with respect to time satisfied in Eq. 20:

$$\begin{aligned} \left(\frac{dL}{dt} \right) &= S'_h + E'_h + I'_h + I'_i + R'_h \\ &= \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h + \sigma_h S_h - \\ &\quad \gamma \phi_h I_h E_h - \phi_h E_h - \mu_h E_h + \beta_h S_h + \\ &\quad \phi_h E_h - (\mu_h + \delta_h) I_h + \gamma \phi_h I_h E_h - \\ &\quad (\mu_h + \varphi_h) I_i + \delta_h I_h + \mu_h I_i - \mu_h R_h \\ &= \mu_h N_h - \mu_h L(t) \end{aligned} \quad (20)$$

Not difficult to prove that Eq. 21:

$$\frac{dL}{dt} = \mu_h N_h - \mu_h L(t) \leq 0 \text{ for } L \geq N_h \quad (21)$$

Then, from the above equation it is known $dL/dt \leq 0$, that means D is a set of positive invariant. Conversely, by completing the system 12 is obtained that, $0 \leq L(t) \leq N_h + L(0)e^{-\mu_h t}$, which L(0) is the initial condition of L(t).

Therefore, if $t \rightarrow \infty, 0 \leq L(t) \leq N_h$ and concluded that D is a set of positive invariant and cover all of the settlement in R_+^5 . This proves the theorem.

This theorem guarantees the existence of TB disease in an area that was initially not found a virus carrier TB bacteria then changed after the discovery of the population suspected but not yet infected, $S_h(t) > 0$, exposed TB $R_h(t) > 0$ infected TB, $I_h(t) > 0$, infected TB by people who have a positive TB, $I_i(t) > 0$ recovered TB, $R_h(t) > 0$. This theorem also gives the conclusion that further investigation of TB cases this stage so that it can identify the stage of disease spread TB endemic to the stage using a SEIR model.

Global stability analysis of the SIR and SEIR model: The basic reproduction number R_0 of the system found by using the method of Side¹⁷ and Diekmann *et al.*¹⁸, R_0 for the system are in Eq. 22:

$$R_0 = \alpha \eta \mu_h \quad (22)$$

For SIR model and SEIR model is in Eq. 23:

$$R_0 = \mu_h \xi \eta \alpha \quad (23)$$

With $\xi = \mu_h + \phi_h$, $\alpha = \mu_h + \delta_h$ and $\eta = \mu_h + \varphi_h$

Global stability of disease-free equilibrium for SIR model:

System 5 always has a disease-free equilibrium $P^* = (S_h^*, I_h^*, S_i^*, R_h^*) = (N_h, 0, 0, 0)$, which means the disease will disappear. This section will examine the behavior of the global balance of disease-free for the system 5.

Theorem 3: If $R_0 \leq 1$, then the disease-free equilibrium P^* for SIR model SIR is stable asymptotic global stage in D.

Proof: Suppose candidate Lyapunov function is in Eq. 24:

$$V(t) = (S_h - S_h^* \ln S_h) + I_h + I_i + R_h \quad (24)$$

By differentiating function of time obtained by the following in Eq. 25:

$$\begin{aligned} \dot{V}(t) &= S_h' \left(1 - \frac{S_h}{S_h^*} \right) + I_h' + I_i' + R_h' \\ &= (\mu_h N_h - \beta_h S_h - \gamma \phi_h I_h E_h - \mu_h S_h) \\ &\quad \left(1 - \frac{S_h}{S_h^*} \right) + \beta_h S_h - (\mu_h + \delta_h) I_h + \\ &\quad \gamma \beta_h I_h S_h - (\mu_h + \phi_h) I_i + \delta_h I_h + \phi_h I_i - \mu_h R_h \\ &= \mu_h N_h \left(1 - \frac{S_h}{S_h^*} \right) + \mu_h S_h^* \left(1 - \frac{S_h}{S_h^*} \right) + \beta_h S_h - \mu_h I_h - \mu_h I_i - \mu_h R_h \end{aligned} \quad (25)$$

Using terms $\beta_h = 0$ and $S_h^* = N_h$, Eq. 25 can be rewritten as:

$$\begin{aligned} \dot{V}(t) &= \mu_h N_h \left(1 - \frac{S_h}{S_h^*} \right) + \mu_h N_h \left(1 - \frac{S_h}{S_h^*} \right) - \mu_h I_h - \mu_h I_i \\ \dot{V}(t) &= \mu_h N_h \left(2 - \frac{S_h}{S_h} - \frac{S_h}{S_h^*} \right) - \mu_h I_h - \mu_h I_i - \mu_h R_h \\ &= -\mu_h N_h \frac{(S_h - S_h^*)^2}{S_h S_h^*} - \mu_h I_h - \mu_h I_i - \mu_h R_h \end{aligned} \quad (26)$$

Therefore, $\dot{V}(t) \leq 0$ by using advanced LaSalle¹⁹ on Lyapunov theorem, finite set of defined each settlement is contained in the largest invariant set $S_h = S_h^*, R_h = 0$ is a singleton $\{P^*\}$. This means that the disease-free equilibrium P^* is the global stage is a stable asymptotic in D. This concludes the proof.

Global stability theorem SIR model explains about the stage rather than the presence of TB cases as described in theorem 1. This step explains that if an individual is infected with TB but $R_0 \leq 1$. It means will not cause another individual infected. This means that in the region TB disease can still be controlled and are at that stage is not alarming.

Global stability of disease-free equilibrium for SEIR model:

System 12 always has a disease-free equilibrium $P^* = (S_h^*, E_h^*, I_h^*, I_i^*, R_h^*) = (N_h, 0, 0, 0, 0)$ which means the disease will disappear. This section will examine behavior of global balance of disease-free for system.

Theorem 4: If $R_0 \leq 1$, then the disease-free equilibrium P^* for SIR model SEIR is stable asymptotic global stage in D.

Proof: Suppose candidate Lyapunov function is in Eq. 27:

$$W(t) = (S_h - S_h^* \ln S_h) + E_h + I_h + I_i + R_h \quad (27)$$

By differentiating function of time obtained by the following Eq. 28:

$$\begin{aligned} \dot{W}(t) &= S_h' \left(1 - \frac{S_h}{S_h^*} \right) + E_h' + I_h' + I_i' + R_h' \\ \dot{W}(t) &= \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h + \mu_h N_h \frac{S_h}{S_h^*} - \\ &\quad (\sigma_h + \beta_h + \mu_h) S_h^* + \sigma_h S_h - (\gamma \phi_h I_h + \phi_h + \mu_h) E_h \\ &\quad - \beta_h S_h + \phi_h E_h - (\delta_h + \mu_h) I_h + \gamma \phi_h I_h E_h - \\ &\quad (\phi_h + \mu_h) I_i + \delta_h I_h + \mu_h I_i - \mu_h R_h \end{aligned} \quad (28)$$

Using terms $\beta_h = \sigma_h = 0$ and $S_h^* = N_h$, Eq. 28 can be rewritten as in Eq. 29:

$$\begin{aligned} \dot{W}(t) &= \mu_h N_h \left(1 - \frac{S_h}{S_h} \right) + \mu_h N_h \left(1 - \frac{S_h}{S_h^*} \right) - \mu_h E_h - \mu_h I_h - \mu_h I_i \\ \dot{W}(t) &= \mu_h N_h \left(2 - \frac{S_h}{S_h} - \frac{S_h}{S_h^*} \right) + \mu_h (E_h + I_h + I_i + R_h) \\ &= \mu_h N_h \frac{(S_h - S_h^*)^2}{S_h S_h^*} - \mu_h (E_h + I_h + I_i + R_h) \end{aligned} \quad (29)$$

Therefore, $\dot{W}(t) \leq 0$ and by using advanced LaSalle¹⁹ on Lyapunov theorem, finite set of defined each settlement is contained in the largest invariant set $S_h = S_h^*, R_h = 0$ is a singleton $\{P^*\}$. This means that the disease-free equilibrium P^* is the global stage is a stable asymptotic in D. This concludes the proof.

Global stability theorem for this SEIR the model describes the stages of the existence of TB cases as described in theorem 2. This step explains that if an individual is infected with TB but $R_0 \leq 1$. It means it will not cause other individuals infected. This means that in the region TB disease can still be controlled and are at that stage is not alarming.

Global stability of the endemic equilibrium for SIR model:

Simplify the SIR model of the system of Eq. 5 to obtain the following Eq. 30:

$$\begin{aligned} \frac{dS_h}{dt} &= \mu_h N_h - \beta_h S_h - \gamma \beta_h I_h S_h - \mu_h S_h \\ \frac{dI_h}{dt} &= \beta_h S_h - (\mu_h + \delta_h) I_h \\ \frac{dI_i}{dt} &= \gamma \beta_h I_h S_h - (\mu_h + \varphi_h) I_i \end{aligned} \quad (30)$$

System 30 has an equilibrium point $P^{**} = (S_h^{**}, I_h^{**}, I_i^{**}) \in D$ called endemic equilibrium and satisfied $S_h^{**} > 0, I_h^{**} > 0, I_i^{**} > 0$ with:

$$\begin{aligned} S_h^{**} &= \frac{-(\mu_h + \beta_h)\alpha + \sqrt{(\beta_h^2 + \mu_h^2)\alpha^2 + 2\mu_h\beta_h\alpha(\alpha + \gamma\beta_h)}}{2\gamma\beta_h^2} \\ I_h^{**} &= \frac{\beta_h \left(-(\mu_h + \beta_h)\alpha + \sqrt{(\beta_h^2 + \mu_h^2)\alpha^2 + 2\mu_h\beta_h\alpha(\alpha + \gamma\beta_h)} \right)}{2\gamma\alpha\beta_h^2} \end{aligned}$$

and:

$$I_i^{**} = \frac{\mu_h + \left((\mu_h + \beta_h)^2 \alpha - (\mu_h + \beta_h) \sqrt{(\beta_h^2 + \mu_h^2)\alpha^2 + 2\mu_h\beta_h\alpha(\alpha + \gamma\beta_h)} \right)}{2\gamma\eta\beta_h^2}$$

The following theorem gives a global explanation of the endemic equilibrium system 30.

Theorem 5: If $R_0 > 1$ then the positive equilibrium state of the system are endemic 30 exists and asymptotic global stage is stable on D, with the assumption that in Eq. 31:

$$\begin{cases} (\delta_h + \mu_h) = \frac{\beta_h S_h^{**}}{I_h^{**}} \\ S_h = S_h^{**} \\ (\varphi_h + \mu_h) = \frac{\gamma I_h^{**} \beta_h S_h^{**}}{I_i^{**}} \end{cases} \quad (31)$$

with $(\delta_h + \mu_h)$ are the rate of infected 1 to recovered human and the rate of birth/death human population and also $(\varphi_h + \mu_h)$ are the rate of infected 2 to recovered human and the rate of birth/death human population.

Proof: Suppose a Lyapunov function is in Eq. 32:

$$V(t) = (S_h - S_h^{**} \ln S_h) + (I_h - I_h^{**} \ln I_h) + (I_i - I_i^{**} \ln I_i) \quad (32)$$

Derive the Eq. 32 to obtain Eq. 33 the following:

$$\begin{aligned} \dot{V}(t) &= S'_h \left(1 - \frac{S_h^{**}}{S_h} \right) + I'_h \left(1 - \frac{I_h^{**}}{I_h} \right) + I'_i \left(1 - \frac{I_i^{**}}{I_i} \right) \\ \dot{V}(t) &= \mu_h N_h \left(1 - \frac{S_h^{**}}{S_h} \right) + \mu_h S_h^{**} \left(1 - \frac{S_h^{**}}{S_h} + \right) \beta_h S_h^{**} \left(1 - \frac{S_h^{**} I_h^{**}}{S_h I_h} \right) + \gamma \beta_h I_h S_h^{**} \\ &\quad \left(1 - \frac{S_h^{**} I_i^{**}}{S_h I_i} \right) + (\mu_h + \delta_h) I_h^{**} \left(1 - \frac{I_h^{**}}{I_h} \right) + (\mu_h + \varphi_h) I_i^{**} \left(1 - \frac{I_i^{**}}{I_i} \right) \end{aligned} \quad (33)$$

Substitution assumption in Eq. 31 into Eq. 33 is obtained Eq. 34:

$$\begin{aligned} \dot{V}(t) &= \beta_h S_h^{**} \left(1 - \frac{I_h^{**}}{I_h} + 1 - \frac{I_h^{**}}{I_h^{**}} \right) + \gamma \beta_h I_h S_h^{**} \left(1 - \frac{I_i^{**}}{I_i} + 1 - \frac{I_i^{**}}{I_i^{**}} \right) \\ &= -\beta_h S_h^{**} \left(\frac{(I_h - I_h^{**})^2}{I_h I_h^{**}} \right) - \gamma \beta_h I_h S_h^{**} \left(\frac{(I_i - I_i^{**})^2}{I_i I_i^{**}} \right) \end{aligned} \quad (34)$$

Equation 34 ensures that, $\dot{V}(t) \leq 0$ for all $(S_h(t), E_h(t), I_h(t), I_i(t)) \in D$ and $\dot{V}(t) \leq 0$ satisfied fulfilled if and only if $S_h = S_h^{**}, I_h = I_h^{**}$ and $I_i = I_i^{**}$.

Then the balance P^{**} is only positive invariant set of system of Eq. 30 are contained entirely within $L = \{(S_h(t), I_h(t), I_i(t)), S_h = S_h^{**}, I_h = I_h^{**}, I_i = I_i^{**}\}$ and subsequently by asymptotic stability theorem¹⁹, a positive balance P^{**} is endemic asymptotic global stage is stable in D. This proves the theorem.

Global stability theorem for SIR models at this stage to explain that if an individual is infected with TB disease, $R_0 > 1$, then that individual will transmit the virus to other individuals. This means that at this stage of TB disease is endemic because it no longer can be controlled and is at an alarming stage, thus becoming a threat to the human population in the area.

Global stability of the endemic equilibrium for SEIR model:

Simplify SEIR model in the system of Eq. 12 obtain the following Eq. 35:

$$\frac{dS_h}{dt} = \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h$$

$$\frac{dE_h}{dt} = \sigma_h S_h - \gamma \phi_h I_h E_h - \phi_h E_h - \mu_h E_h$$

$$\frac{dI_h}{dt} = \beta_h S_h + \phi_h E_h - (\mu_h + \delta_h) I_h \quad (35)$$

$$\frac{dI_i}{dt} = \gamma \phi_h I_h E_h - (\mu_h + \phi_h) I_i$$

System 35 has a equilibrium point $P^{**} = (S_h^{**}, E_h^{**}, I_h^{**}, I_i^{**}) \in D$ known as endemic equilibrium and satisfied $S_h^{**} > 0, E_h^{**} > 0, I_h^{**} > 0, I_i^{**} > 0$ with:

$$E_h^{**} = \frac{\sqrt{T(T\beta_h^2 + 4U + 2\beta_h V) + V^2 - T\beta_h - V}}{2\gamma\phi_h^2(\mu_h + \beta_h + \sigma_h)}$$

$$T = \gamma\mu_h\phi_h$$

$$U = \sigma_h\phi_h(\mu_h + \delta_h)(\mu_h + \beta_h + \sigma_h)$$

$$V = (\mu_h + \delta_h)(\mu_h + \phi_h)(\mu_h + \beta_h + \sigma_h)$$

$$S_h^{**} = \frac{\mu_h}{(\mu_h + \beta_h + \sigma_h)}, I_h^{**} = \frac{\mu_h\beta_h + \phi_h(\mu_h + \beta_h + \sigma_h)E_h^{**}}{(\mu_h + \delta_h)(\mu_h + \beta_h + \sigma_h)}$$

and:

$$I_i^{**} = \frac{\mu_h\sigma_h - (\mu_h + \phi_h)(\mu_h + \beta_h + \sigma_h)E_h^{**}}{(\mu_h + \phi_h)(\mu_h + \beta_h + \sigma_h)}$$

The following theorem will provide a global explanation of endemic equilibrium 35.

Theorem 6: If $R_0 > 1$, then the positive equilibrium state of endemic system 35 exists and asymptotic global stage is stable on D, with the assumption that in Eq. 36:

$$\left\{ \begin{array}{l} (\delta_h + \mu_h) = \frac{\beta_h S_h^{**} + \phi_h E_h}{I_h^{**}} \\ S_h = S_h^{**} \\ E_h = E_h^{**} \\ (\phi_h + \mu_h) = \frac{\gamma I_h \phi_h S_h^{**}}{I_i^{**}} \end{array} \right. \quad (36)$$

with $(\delta_h + \mu_h)$ are the rate of infected 1 to recovered human and the rate of birth/death human population and also $(\phi_h + \mu_h)$ are the rate of infected 2 to recovered human and the rate of birth/death human population.

Proof: Suppose a Lyapunov function in Eq. 37 is:

$$W(T) = (S_h - S_h^{**} \ln S_h) + (E_h - E_h^{**} \ln E_h) + (I_h - I_h^{**} \ln I_h) + (I_i - I_i^{**} \ln I_i) \quad (37)$$

Derive the Eq. 37 to obtain 38 the following:

$$\dot{W}(t) = S_h' \left(1 - \frac{S_h^{**}}{S_h} \right) - E_h' \left(1 - \frac{E_h^{**}}{E_h} \right) + I_h' \left(1 - \frac{I_h^{**}}{I_h} \right) + I_i' \left(1 - \frac{I_i^{**}}{I_i} \right)$$

$$\begin{aligned} \dot{W}(t) = & \mu_h N_h - (\sigma_h + \beta_h + \mu_h) S_h - \mu_h N_h \frac{S_h^{**}}{S_h} + \\ & (\sigma_h + \beta_h + \mu_h) S_h^{**} + \sigma_h S_h - \gamma I_h \phi_h E_h - \\ & - (\mu_h - \phi_h) E_h - \sigma_h S_h \frac{E_h^{**}}{E_h} + \gamma I_h \phi_h E_h^{**} + \\ & (\mu_h + \phi_h) E_h^{**} \beta_h S_h + \phi_h E_h - (\mu_h + \delta_h) I_h - \beta_h S_h \frac{I_h^{**}}{I_h} - \\ & \phi_h E_h \frac{I_h^{**}}{I_h} + (\mu_h + \delta_h) I_h^{**} \end{aligned}$$

Then it have:

$$\begin{aligned} \dot{W}(t) = & \mu_h N_h \left(1 - \frac{S_h^{**}}{S_h} \right) + \mu_h S_h^{**} \left(1 - \frac{S_h}{S_h^{**}} \right) \\ & \sigma_h S_h^{**} \left(1 - \frac{E_h^{**}}{E_h} \right) + \beta_h S_h^{**} \left(1 - \frac{S_h I_h^{**}}{S_h^{**} I_h} \right) \\ & + \gamma \phi_h I_h E_h^{**} + \left(1 - \frac{E_h I_i^{**}}{E_h^{**} I_i} \right) + \gamma I_h \phi_h E_h \\ & - (\mu_h + \phi_h) I_i - \gamma I_h \phi_h E_h \frac{I_i^{**}}{I_i} + \\ & (\mu_h + \phi_h) I_i^{**} + \phi_h E_h^{**} \left(1 - \frac{E_h I_h^{**}}{E_h^{**} I_h} \right) + \\ & \mu_h E_h^{**} \left(1 - \frac{E_h}{E_h^{**}} \right) + (\mu_h + \delta_h) I_h^{**} \\ & \left(1 - \frac{I_h}{I_h^{**}} \right) + (\mu_h + \phi_h) I_i^{**} \left(1 - \frac{I_i}{I_i^{**}} \right) \end{aligned} \quad (38)$$

Substitution assumption in Eq. 36 into Eq. 38 is obtained Eq. 39:

$$\begin{aligned} \dot{W}(t) = & (\mu_h + \delta_h) I_h^{**} \left(1 - \frac{I_h}{I_h^{**}} \right) + (\beta_h S_h^{**} + \phi_h E_h^{**}) \\ & \left(1 - \frac{I_h}{I_h^{**}} \right) + (\mu_h + \phi_h) I_i^{**} \left(1 - \frac{I_h}{I_h^{**}} \right) + \\ & \gamma \phi_h I_h E_h^{**} \left(1 - \frac{I_h^{**}}{I_i} \right) \\ = & -(\beta_h S_h + \phi_h E_h) \frac{(I_h - I_h^{**})^2}{I_h I_h^{**}} - \gamma \phi_h I_h E_h \left(\frac{(I_i - I_i^{**})^2}{I_i I_i^{**}} \right) \end{aligned} \quad (39)$$

Equation 39 ensures that $\dot{W}(t) \leq 0$ for all $(S_h(t), E_h(t), I_h(t), I_i(t)) \in D$ and $\dot{W}(t) = 0$ fulfilled if and only if $S_h = S_h^{**}, E_h = E_h^{**}, I_h = I_h^{**}$ and $I_i = I_i^{**}$.

Then the balance P^{**} is only positive invariant set of system of Eq. 35 are contained entirely within $L = \{(S_h(t), E_h(t), I_h(t), I_i(t)), S_h = S_h^{**}, E_h = E_h^{**}, I_h = I_h^{**}, I_i = I_i^{**}\}$ and subsequently by asymptotic stability theorem¹⁹, endemic positive balance P^{**} is endemic asymptotic global stage is stable in D. This proves the theorem.

Global stability theorem for SEIR model at this stage to explain that if an individual is infected with TB disease $R_0 > 1$, then that individual will transmit the virus to other individuals. This means that at this stage of TB disease is endemic because it no longer can be controlled and is at an alarming stage, thus becoming a threat to the human population in the region.

Korobeinikov²⁰ and Korobeinikov and Maini²¹ have used the Lyapunov function method for SEIR and SEIS epidemic models. Syafruddin and Noorani⁷ and Tewa *et al.*¹⁵ have used the Lyapunov function method for SIR and SEIR model dengue fever disease. Side¹⁷ has made mathematical modeling SIR for tuberculosis disease but has not discussed the SEIR model, global stability and the Lyapunov function method. In this study, Lyapunov function method is used to SIR and SEIR model for Tuberculosis disease.

CONCLUSION

This study is acquired two mathematical models in TB transmission is SIR and SEIR. Both models were analyzed using Lyapunov function to explain the stability of the global TB disease. The first and second theorem explains the existence of TB disease in the region. The third and fourth theorem describes TB disease-free equilibrium, when the basic reproduction number $R_0 \leq 1$ and the two last theorem describes endemic TB disease, when the basic reproduction number $R_0 > 1$. All of theorem has been proved using Lyapunov function.

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