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MATHEMATICAL ANALYSIS OF A TUBERCULOSIS MODEL WITH TWO DIFFERENT STAGES OF INFECTION

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Tuberculosis is an infectious disease. This disease causes death and the world notes that Tuberculosis has a high mortality rate. A mathematical model of Tuberculosis with two infection stages of individuals, pre infected and actively infected, is studied in this paper. The rate of treatment considered in this model. The stability analysis of the equilibrium is determined by the basic reproduction ratio. Routh Hurwitz linearization is used for investigate the local stability of uninfected equilibrium. While the global stability of endemic equilibrium is investigated by construct Lyapunov function. The effect of treatment in pre infected and actively infected stages can reduce the spread rate of Tuberculosis as shown in numerical simulation.
Keywords: Tuberculosis, Treatment Effectiveness, Stability, Equilibrium

I. INTRODUCTION

Tuberculosis is one of the most deadly infectious diseases [1,2]. One in three persons across the world representing 2–3 billion individuals are known to be infected with Mycobacterium Tuberculosis (M. tuberculosis) of which 5–15% are likely to develop active tuberculosis disease during their lifetime [3]. In 2014, an estimated 9.6 million people fell ill due to tuberculosis, around 1.5 million people died from the disease including 1.1 million HIV-negative persons and 400,000 HIV patients [3]. Tuberculosis usually affects the lungs, but it can also affect the brain, the kidneys, or the spine. Tuberculosis is spread through the air. When a person with tuberculosis disease coughs or sneezes, droplet nuclei containing M. tuberculosis are expelled into the air. If another person inhales air containing these droplet nuclei, he or she may become infected. [4,5]

Not everyone infected with tuberculosis bacterium becomes sick. They remain in the inactive (pre infected) tuberculosis stage. Pre infection means the person has the presence of immune responses to bacterium infection without clinical explanation of active tuberculosis [3,4,5]. The vast majority of infected individuals have no signs of tuberculosis disease and are not infectious, but they are at risk for developing active tuberculosis disease and becoming infectious [5]. Some will develop active tuberculosis anytime from months to years after being exposed [5,6,7]. However, the likelihood of progression of pre infection to active tuberculosis depends on bacterial, host, and environmental factors [5]. Treatment can prevent the development of disease.

Mathematical modelling has provided tools to understanding the dynamics of the spread of tuberculosis. Some studies have developed mathematical models of the spread of tuberculosis. Bowong and Tewa [10] modelled dynamics of SEI type of tuberculosis with a rate of general contact. In that model, stability of equilibrium was analysed by Lyapunov function and LaSalle's invariant set theorem. Another model from Bowong and Tewa [11] is SEIL type of tuberculosis. Unmonitored individuals in L (Loss of sight) stage was considered, where in this stage there is no information about their health. The global dynamics of the model is solved by Lyapunov function. Huo and Zou [13] presented a SEIR model with considering symptomatic infectious individuals treated at home and treated in the hospital. The existence and uniqueness of equilibrium are derived and the global stability of equilibrium are also proved.

We propose and analyze a model to study the effectiveness of treatment in controlling the spread of tuberculosis during two different stage of infection, pre infected and actively infected. We study the dynamical behaviour of the model, including the existence and stability of equilibrium for the model, and present the evolution of susceptible, exposed, pre infected and actively infected subpopulation in long terms.

II. MODEL FORMULATION

The model consists of four variable and several parameters. The model form five nonlinear equations describing populations of susceptible (S), exposed (E), pre infected (I_1), and actively infected (I_2). The mathematical model can be presented in the following

$$\frac{dS}{dt} = \lambda - \beta_1 p I_1 S - \beta_2 q I_2 S - \mu S \tag{1}$$

$$\frac{dE}{dt} = \beta_1 p I_1 S + \beta_2 q I_2 S - (\mu + \alpha) E + \gamma r I_2 \tag{2}$$

$$\frac{dI_1}{dt} = \alpha E - (\mu + \delta_1 + \omega) I_1 + \gamma (1 - r) I_2 \tag{3}$$

$$\frac{dI_2}{dt} = \omega I_1 - (\mu + \delta_2 + \gamma) I_2 \tag{4}$$

The recruitment rate of the susceptible population is λ. Parameter μ represents the natural mortality rate. Parameter β_1 and β_2 are transmission rate with I_1 and I_2 respectively. The fraction of susceptible individuals go to pre infected and actively infected stages are denoted by *p, q* respectively. We denote α as the rate of change of exposed subpopulation enter pre infected stage. The rate of change of an individual from the pre infected stage to the actively infected stage is denoted by ω. By δ_1 and δ_2 we denote the death rate due to pre-tuberculosis and active tuberculosis, respectively. An actively infected individual is given the treatment γr, after that he will have two possibilities, either he will go to exposed stage or he will become pre infected. While the fraction $\gamma(1-r)$ of the infectious stage I_2 move to infectious stage I_1.

III. ANALYSIS OF THE MODEL

In this section, we study the basic reproduction ratio and explore the stability of uninfected state, and stability of endemic equilibrium of the model (1) – (4) .

3.1 Basic Reproduction Ratio

We derive the basic reproduction ratio, $\Re_0$, using the next generation matrix. It is straightforward to see that the model (1) – (4) has an uninfected equilibrium point $UE = \left(\frac{\lambda}{\mu}, 0, 0, 0\right)$. From Dickmann [15], we can obtain the basic reproduction ratio $\Re_0$ for system (1) – (4) as follows,

$$\Re_0 = \frac{\lambda\alpha\left[p\left(\mu+\delta_2+\gamma\right)\beta_1 + q\omega\beta_2\right]}{\mu\left[\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right]} \qquad (6)$$

Next, the local stability of uninfected equilibrium is presented in the following subsection.

3.2 Local Stability of Uninfected Equilibrium

The local stability of the model (1) – (4) can be proved by using linearization Routh- Hurwitz criterion.

Theorem 1: If $\Re_0 < 1$, the uninfected equilibrium $UE = \left(\frac{\lambda}{\mu}, 0, 0, 0\right)$ is locally asymptotically stable.

Proof: The system (1) – (4) has Jacobian matrix at $UE = \left(\frac{\lambda}{\mu}, 0, 0, 0\right)$ in the following,

$$J\left(UE\right) = \begin{bmatrix} -\mu & 0 & -\beta_1 p\frac{\lambda}{\mu} & -\beta_2 q\frac{\lambda}{\mu} \\ 0 & -\left(\mu+\alpha\right) & \beta_1 p\frac{\lambda}{\mu} & \beta_2 q\frac{\lambda}{\mu}+\gamma r \\ 0 & \alpha & -\left(\mu+\delta_1+\omega\right) & \gamma\left(1-r\right) \\ 0 & 0 & \omega & -\left(\mu+\delta_2+\gamma\right) \end{bmatrix} \qquad (7)$$

The Jacobian matrix (7) has four eigenvalues, they are $-\mu$ and the solution of the polynomial equation

$$\zeta^3 + A_2\zeta^2 + A_1\zeta + A_0 = 0,$$

where,

$A_2 = 3\mu+\alpha+\gamma+\omega+\delta_1+\delta_2$,

$$A_1 = \frac{\left(\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right)p\beta_1}{p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2}\left(1-\Re_0\right)+$$

$$\frac{p\left(\left(\mu+\delta_2+\gamma\right)^2\left(2\mu+\alpha+\delta_1\right)+\left(\mu+\delta_2\right)^2\omega+\gamma\omega\left(2\mu+\alpha+\delta_2+r\left(\delta_2+\gamma\right)\right)\right)}{p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2}\beta_1+$$

$$\frac{q\omega\left(\left(\mu+\delta_2+\gamma\right)\left(2\mu+\alpha+\delta_1\right)+\left(\mu+\delta_1\right)\left(\mu+\alpha\right)+\omega\left(2\mu+\alpha+\delta_2+\gamma r\right)\right)}{p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2}\beta_2$$

$$A_0=\left(\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right)\left(1-\Re_0\right)$$

By manipulating the computation $A_1A_2-A_0$, we have

$$A_1A_2-A_0=\left(\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right)\left(1-\Re_0\right)$$

$$\left(\frac{\left(2\mu+\alpha+\delta_1+\omega\right)p\beta_1-q\omega\beta_2}{p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2}\right)+\frac{A_1}{p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2}$$

$$\left[p\left(\left(\mu+\delta_2+\gamma\right)^2\left(2\mu+\alpha+\delta_1\right)+\left(\mu+\delta_2\right)^2\omega+\gamma\omega\left(2\mu+\alpha+\delta_2+r\left(\delta_2+\gamma\right)\right)\right)\beta_1+\right.$$

$$\left.q\omega\left(\left(\mu+\delta_2+\gamma\right)\left(2\mu+\alpha+\delta_1\right)+\left(\mu+\delta_1\right)\left(\mu+\alpha\right)+\omega\left(2\mu+\alpha+\delta_2+\gamma r\right)\right)\beta_2\right]$$

We see that $A_1A_2-A_0>0$, when $\Re_0<1$. Based on Routh-Hurwitz criterion, it is proven that uninfected equilibrium $UE=\left(\frac{\lambda}{\mu},0,0,0\right)$ is locally asymptotically stable when $\Re_0<1$. □

3.3 Global Stability for the Endemic Equilibrium

We construct Lyapunov function to investigate the global stability for the endemic equilibrium. The model (1) – (4) has endemic equilibrium $EE=\left(S^*,E^*,I_1{}^*,I_2{}^*\right)$, where

$$S^*=\frac{\lambda\omega}{\beta_1p\left(\mu+\delta_2+\gamma\right)I_2+\beta_2q\omega I_2+\mu\omega},$$

$$E^*=\frac{\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\delta_2\right)\omega+\gamma_2r\omega}{\alpha\omega},$$

$$I_1^*=\frac{I_2\left(\mu+\delta_2+\gamma\right)}{\omega}.$$

The equilibrium point $I_2{}^*$ satisfied the linear equation

$$a_1I_2+a_0=0 \qquad (8)$$

where,

$$a_1=\left(p\left(\mu+\delta_2+\gamma\right)\beta_1+q\omega\beta_2\right)\left(\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right),$$

$$a_0=\mu\omega\left(\left(\mu+\alpha\right)\left(\mu+\delta_1\right)\left(\mu+\delta_2+\gamma\right)+\left(\mu+\alpha\right)\left(\mu+\delta_2\right)\omega+\mu\omega\gamma r\right)\left(1-\Re_0\right).$$

The equation (8) has exactly one positive solution $I_2{}^*$ if and only if $\frac{a_0}{a_1}<1$ or $\Re_0>1$. As a result, the endemic equilibrium exists when $\Re_0>1$. Later, Theorem 2 gives the global stability for the endemic equilibrium.

Theorem 2: If $\Re_0 > 1$, the endemic equilibrium $EE = \left(S^*, E^*, I_1{}^*, I_2{}^*\right)$ of the system (1) - (4) is globally asymptotically stable.

Proof: Consider a Lyapunov function, $F \in C^1$, as follows,

$$F = \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + c_1\left(E - E^* - E^* \ln \frac{E}{E^*}\right) + c_2\left(I_1 - I_1{}^* - I_1{}^* \ln \frac{I_1}{I_1{}^*}\right)$$
$$+ c_3\left(I_2 - I_2^* - I_2{}^* \ln \frac{I_2}{I_2^*}\right)$$

where c_1, c_2, c_3 are positive constant. The type of Lyapunov function that we used has been mentioned in [18], [19], [20], [21], [22]. Derivative of F with respect to t is given as follows

$$\begin{aligned}\frac{dF}{dt} &= \left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + c_1\left(1 - \frac{E^*}{E}\right)\frac{dE}{dt} + c_2\left(1 - \frac{I_1^*}{I_1^*}\right)\frac{dI_1^*}{dt} + c_3\left(1 - \frac{I_2^*}{I_2^*}\right)\frac{dI_2^*}{dt} \\ &= \left(\lambda + \mu S^* + c_1(\mu+\alpha)E^* + c_2(\mu+\delta_1+\omega)I_1^* + c_3(\mu+\delta_2+\gamma)I_2{}^*\right) \\ &\quad + \left(-\beta_1 p I_1 S - \beta_2 q I_2 S - \mu S\right) - \left(\lambda\frac{S^*}{S} - \beta_1 p I_1 S^* - \beta_2 q I_2 S^*\right) + \left(c_1\beta_1 p I_1 S + \right. \\ &\quad \left. c_1\beta_2 q I_2 S - c_1(\mu+\alpha)E + c_1\gamma r I_2\right) - \left(c_1\beta_1 p I_1 S\frac{E^*}{E} + c_1\beta_2 q I_2 S\frac{E^*}{E}\right. \qquad (9) \\ &\quad \left. + c_1\gamma r I_2\frac{E^*}{E}\right) + \left(c_2\alpha E - c_2(\mu+\delta_1+\omega)I_1 + c_2\gamma(1-r)I_2\right) \\ &\quad - \left(c_2\alpha E\frac{I_1^*}{I_1} + c_2\gamma(1-r)I_2\frac{I_1^*}{I_1}\right) + \left(c_3\omega I_1 - c_3(\mu+\delta_2+\gamma)I_2\right) - \left(c_3\omega I_1\frac{I_2^*}{I_2}\right)\end{aligned}$$

By considering

$$\lambda = \beta_1 p I_1{}^* S^* + \beta_2 q I_2{}^* S^* + \mu S^* \qquad (10)$$
$$(\mu+\alpha)E^* = \beta_1 p I_1{}^* S^* + \beta_2 q I_2{}^* S^* + \gamma r I_2{}^* \qquad (11)$$
$$(\mu+\delta_1+\omega)I_1{}^* = \alpha E^* + \gamma(1-r)I_2{}^* \qquad (12)$$
$$(\mu+\delta_2+\gamma)I_2{}^* = \omega I_1{}^* \qquad (13)$$

The equation (9) becomes

$$\begin{aligned}\frac{dF}{dt} &= \mu S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \beta_1 p I_1{}^* S^*\left(1 - \frac{S^*}{S}\right) + \beta_2 q I_2{}^* S^*\left(1 - \frac{S^*}{S}\right) + \\ &\quad c_1\beta_1 p I_1{}^* S^*\left(1 - \frac{I_1}{I_1{}^*}\frac{S}{S^*}\frac{E^*}{E}\right) + c_1\beta_2 q I_2{}^* S^*\left(1 - \frac{I_2}{I_2{}^*}\frac{S}{S^*}\frac{E^*}{E}\right) + c_1\gamma r I_2{}^*\left(1 - \frac{I_2}{I_2{}^*}\frac{E^*}{E}\right) \\ &\quad + c_2\alpha E^*\left(1 - \frac{E}{E^*}\frac{I_1{}^*}{I_1}\right) + c_2\gamma(1-r)I_2{}^*\left(1 - \frac{I_2}{I_2{}^*}\frac{I_1{}^*}{I_1}\right) + c_3\omega I_1{}^*\left(1 - \frac{I_1}{I_1{}^*}\frac{I_2{}^*}{I_2}\right) + \qquad (14) \\ &\quad \left(c_2\alpha - c_1(\mu+\alpha)\right)E + \left(\beta_1 p S^* + c_3\omega - c_2(\mu+\delta_1+\omega)\right)I_1 + \left(\beta_2 q S^* + c_1\gamma r + \right. \\ &\quad \left. c_2\gamma(1-r) - c_3(\mu+\delta_2+\gamma)\right)I_2 + \left(-\beta_1 p + c_1\beta_1 p\right)I_1 S + \left(-\beta_2 q + c_1\beta_2 q\right)I_2 S\end{aligned}$$

We denote $x=\frac{S}{S^*}, y=\frac{E}{E^*}, w=\frac{I_1}{I_1^*}, z=\frac{I_2}{I_2^*}$. The equation (14) becomes

$$\begin{aligned}\frac{dF}{dt}=&\mu S^*\left(2-x-\frac{1}{x}\right)+\beta_1 pI_1{}^*S^*\left(1-\frac{1}{x}\right)+\beta_2 qI_2{}^*S^*\left(1-\frac{1}{x}\right)+c_1\beta_1 pI_1{}^*S^*\left(1-\frac{xw}{y}\right)+\\&c_1\beta_2 qI_2{}^*S^*\left(1-\frac{xz}{y}\right)+c_1\gamma rI_2{}^*\left(1-\frac{z}{y}\right)+c_2\alpha E^*\left(1-\frac{y}{w}\right)+c_3\omega I_1{}^*\left(1-\frac{w}{z}\right)+\\&c_2\gamma(1-r)I_2{}^*\left(1-\frac{z}{w}\right)+\left(c_2\alpha-c_1(\mu+\alpha)\right)E+\left(\beta_1 pS^*+c_3\omega-c_2(\mu+\delta_1+\omega)\right)I_1\\&+\left(\beta_2 qS^*+c_1\gamma r+c_2\gamma(1-r)-c_3(\mu+\delta_2+\gamma)\right)I_2+\left(-\beta_1 p+c_1\beta_1 p\right)I_1S+\\&\left(-\beta_2 q+c_1\beta_2 q\right)I_2S\end{aligned}\quad(15)$$

The coefficients of E, I_1, I_2, I_1S, I_2S are made equal to zero, so we have

$$c_1=1 \quad(16)$$

$$c_1(\mu+\alpha)=c_2\alpha \quad(17)$$

$$c_2(\mu+\delta_1+\omega)=\beta_1 pS^*+c_3\omega \quad(18)$$

$$c_3(\mu+\delta_2+\gamma)=\beta_2 qS^*+c_1\gamma r+c_2\gamma(1-r) \quad(19)$$

Substituting equation (16) into equation (15), we have

$$\begin{aligned}\frac{dF}{dt}=&\mu S^*\left(2-x-\frac{1}{x}\right)+c_1\beta_1 pI_1{}^*S^*\left(2-\frac{1}{x}-\frac{xw}{y}\right)+c_1\beta_2 qI_2{}^*S^*\left(2-\frac{1}{x}-\frac{xz}{y}\right)+\\&c_1\gamma rI_2{}^*\left(1-\frac{z}{y}\right)+c_2\alpha E^*\left(1-\frac{y}{w}\right)+c_2\gamma(1-r)I_2{}^*\left(1-\frac{z}{w}\right)+c_3\omega I_1{}^*\left(1-\frac{w}{z}\right)\end{aligned}\quad(20)$$

Equation (11) is multiplied by c_1 and equation (17) is multiplied by E^* gives

$$\begin{cases}c_1(\mu+\alpha)E^*=c_1\beta_1 pI_1{}^*S^*+c_1\beta_2 qI_2{}^*S^*+c_1\gamma rI_2{}^*\\c_1(\mu+\alpha)E^*=c_2\alpha E^*\end{cases}$$

Therefore, it shows that

$$c_1\beta_1 pI_1{}^*S^*+c_1\beta_2 qI_2{}^*S^*+c_1\gamma rI_2{}^*-c_2\alpha E^*=0 \quad(21)$$

Now multiplying equation (21) by $F_1(u)$, where $u=(x,y,w,z)^T$, gives

$$c_1\beta_1 pI_1{}^*S^*F_1(u)+c_1\beta_2 qI_2{}^*S^*F_1(u)+c_1\gamma rI_2{}^*F_1(u)-c_2\alpha E^*F_1(u)=0 \quad(22)$$

Then, equation (12) is multiplied by c_2 and equation (18) is multiplied by $I_1{}^*$ gives

$$\begin{cases}c_2(\mu+\delta_1+\omega)I_1{}^*=c_2\alpha E^*+c_2\gamma(1-r)I_2{}^*\\c_2(\mu+\delta_1+\omega)I_1{}^*=\beta_1 pI_1{}^*S^*+c_3\omega I_1{}^*\end{cases}$$

Therefore, it shows that

$$c_2\alpha E^*+c_2\gamma(1-r)I_2{}^*-\beta_1 pI_1{}^*S^*-c_3\omega I_1{}^*=0 \quad(23)$$

Now, multiplying equation (23) by $F_2(u)$, where $u=(x,y,w,z)^T$, and using equation (16) gives

$$c_2\alpha E^* F_2(u) + c_2\gamma(1-r) I_2{}^* F_2(u) - c_1\beta_1 p I_1{}^* S^* F_2(u) - c_3\omega I_1{}^* F_2(u) = 0 \quad (24)$$

Then, equation (13) is multiplied by c_3 and equation (19) is multiplied by V^* gives

$$\begin{cases} c_3(\mu+\delta_2+\gamma) I_2{}^* = c_3\omega I_1{}^* \\ c_3(\mu+\delta_2+\gamma) I_2{}^* = \beta_2 q I_2{}^* S^* + c_1\gamma r I_2{}^* + c_2\gamma(1-r) I_2{}^* \end{cases}$$

Therefore, it shows that

$$c_3\omega I_1{}^* - \beta_2 q I_2{}^* S^* - c_1\gamma r I_2{}^* - c_2\gamma(1-r) I_2{}^* = 0 \quad (25)$$

Now, multiplying equation (25) by $F_3(u)$, where $u = (x, y, w, z)^T$, and using equation (16) gives

$$c_3\omega I_1{}^* F_3(u) - c_1\beta_2 q I_2{}^* S^* F_3(u) - c_1\gamma r I_2{}^* F_3(u) - c_2\gamma(1-r) I_2{}^* F_3(u) = 0 \quad (26)$$

Thus, after adding equation (22), (24), (26) into equation (20), we obtain

$$\begin{aligned} \frac{dF}{dt} = {} & \mu S^* \left(2 - x - \frac{1}{x}\right) + c_1\beta_1 p I_1{}^* S^* \left(2 - \frac{1}{x} - \frac{xw}{y} + F_1(u) - F_2(u)\right) + \\ & c_1\beta_2 q I_2{}^* S^* \left(2 - \frac{1}{x} - \frac{xz}{y} + F_1(u) - F_3(u)\right) + c_1\gamma_2 r I_2{}^* \left(1 - \frac{z}{y} + F_1(u) - F_3(u)\right) + \\ & c_2\alpha E^* \left(1 - \frac{y}{w} - F_1(u) + F_2(u)\right) + c_2\gamma_2(1-r) I_2{}^* \left(1 - \frac{z}{w} + F_2(u) - F_3(u)\right) + \\ & c_3\omega I_1{}^* \left(1 - \frac{w}{z} - F_2(u) + F_3(u)\right) \end{aligned} \quad (27)$$

Functions $F_1(u)$, $F_2(u)$ and $F_3(u)$ are chosen such that the coefficients of E^* and $I_1{}^*$ are equal to 0. In this case, $F_1(u) - F_2(u) = 1 - \frac{y}{w}$, $F_2(u) - F_3(u) = 1 - \frac{w}{z}$, and $F_1(u) - F_3(u) = 2 - \frac{y}{w} - \frac{w}{z}$.

Then, we get the equation

$$\begin{aligned} \frac{dF}{dt} = {} & \mu S^* \left(2 - x - \frac{1}{x}\right) + c_1\beta_1 p I_1{}^* S^* \left(3 - \frac{1}{x} - \frac{y}{w} - \frac{xw}{y}\right) + c_1\beta_2 q I_2{}^* S^* \left(4 - \frac{1}{x} - \frac{y}{w} - \frac{w}{z} - \frac{xz}{y}\right) \\ & + c_1\gamma r I_2{}^* \left(3 - \frac{z}{y} - \frac{y}{w} - \frac{w}{z}\right) + c_2\gamma(1-r) I_2{}^* \left(2 - \frac{z}{w} - \frac{w}{z}\right) \le 0. \end{aligned} \quad (28)$$

One can see that $\frac{dF}{dt} = 0$ when $S = S^*, E = E^*, I_1 = I_1^*, I_2 = I_2^*$, so the maximal invariant set $\left\{(S, E, I_1, I_2) \mid \frac{dF}{dt} = 0\right\}$ is set of point $\{EE\}$. We conclude that $EE = (S^*, E^*, I_1{}^*, I_2{}^*)$ is globally asymptotically stable. □

IV. NUMERICAL SIMULATION

We illustarate the evolution of susceptible, exposed, pre infected, and actively infected subpopulations by numerical simulation. For the simulation, we use the values of several

parameters, they are $\lambda = 20,\ \beta_1 = 0.0005,\ \beta_2 = 0.0001,\ \mu = 0.014,\ \alpha = 0.25,\ \omega = 0.35,\ \gamma = 0.01,\ \delta_1 = 0.2, \delta_2 = 0.02,\ p = q = r = 0.5,\ \Re_0 = 3.0643 > 1$. Numerical result is given in Figure 1. In Figure 1, it present the change in the number of susceptible, exposed, pre infected, and actively infected subpopulation. The number of susceptible subpopulation increases sharply in the early period and then start decreasing to its equilibrium point after 100 days. The number of exposed subpopulation decreases due to the change in exposed individuals become pre infected individuals. The effectiveness of treatment causing the number of pre infected subpopulation also decreases and going to its equilibrium point. In the actively infected subpopulation, the number of individuals on that stage increase slowly, then decreasing because of the treatment rate. After 50 days, the number of actively infected subpopulation increases again due to the value of $\Re_0$ is greater than one. It means that the disease will remain in the population, and over time the subpopulation will stable towards its equilibrium point.

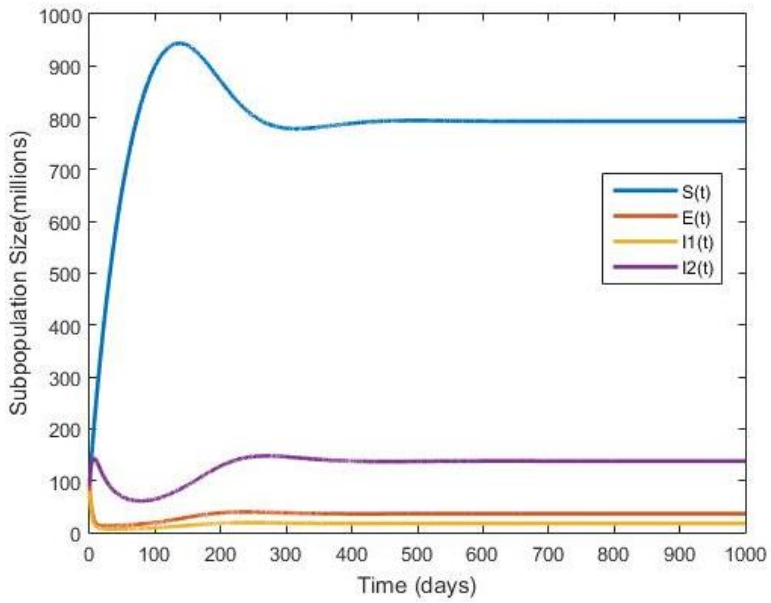

Figure 1. The change of susceptible, exposed, pre infected, and actively infected subpopulation size

V. CONCLUSION

We developed a mathematical model to describe the effectiveness of treatment on dynamical population of tuberculosis during the active infection stage. The model was grouped into susceptible stage, exposed stage, and two different stages of infection, namely pre infected and actively infected. We proved the local stability of uninfected equilibrium and the global stability of endemic equilibrium. The stability depends on the basic reproduction ratio. The ratio is less than one means that the uninfected equilibrium is locally asymptotically stable. We proved the global stability of endemic equilibrium by construct Lyapunov function. For endemic equilibrium, the global stability is achieved when the ratio exceeds one. The number of

susceptible subpopulation increases due to infected individuals. Furthermore, the effectiveness of treatment in two different infection stages can reduce the rate of spread of tuberculosis. Both of equilibrium points were asymptotically stable, so that the population will be stable and converge to a one value.

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