The Stability Analysis of the Mathematical Model of Tuberculosis Transmission Dynamics

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Abstract: ***In this paper, we present the stability analysis of the mathematical model of Tuberculosis transmission dynamics based on SEI model. The analysis is derived from the principles of compartmental modeling showing the rates at which susceptible S move to latent class E and to the infectious class I. We used assumption and schematic presentation to get a system of three non-linear ordinary equations that govern the transmission of the disease guided by the work in [3] The steady state solution was computed and the basic reproduction number R_0 was obtained as $\frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)}$. A stability analysis was done and the disease free equilibrium is shown to be stable if $\frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)} < 1$ and unstable if $\frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)} > 1$.***

Keywords: Latent infection, Stability Analysis, Disease –free equilibrium, Reproduction number and non-linear ordinary equation.

1. Introduction

Tuberculosis (TB) remains a leading cause of infections mortality in the world despite many decade of study, the widespread availability of vaccine, an arsenal of anti-microbial drugs and more recently, a highly visible world health organization (WHO) effort to promote unified global control strategy. It is responsible for approximately two million deaths each year. Recent data released by the health protection agency in 2000 shows that the overall global incidence of the disease in Africa and part of Eastern Europe and Asia[4].

Mathematical modeling has played a vital role in the formulation of TB control strategies and the establishment of interim goals for intervention programs. Most of these models are of the SIR class in which the host population is categorized by infection status as Susceptible, Infectious and Recovered. The principle attributes of this model is the rate at which the Susceptible leave the susceptible class and move into an infected category is a function of the number of infectious hosts in the population at any time t and is thus a non-linear term. Other transition such as the recovery of infectious individuals and the deaths are modeled as linear terms with constant coefficient.

Tuberculosis is caused by infection with bacterium Mycobacterium tuberculosis[3]. The disease is airborne and so it is primarily transmitted through the respiratory route. Individuals with active disease many infect others if the airborne particles they produce when they talk, cough or sneeze or spit are inhaled by others [3]. Once infected, an individual enters a period of latency during which he exhibits no symptoms of the disease and is not infections to others. This latent period can be of extremely variable length of time and the great majority of those infected ie approximately 90% will never have clinical tuberculosis. However, a small proportion of individual progress to disease relatively rapidly falling ill within months or several years after infection [3]. Others may be asymptomatically infected for decade before they become sick. Once ill and infection, individual may recover without treatment, may be cured with antibiotics or may die from the disease. Recovered individuals may relapse to disease or be re-infected.

When the disease become active, 75% of the case involve infection in the lungs (pulmonary tuberculosis) and the symptoms at this level includes chest pain, coughing up of blood and prolonged cough for more than three weeks, systemic symptoms includes: fever, chills, night sweats, appetite loss, weight loss, pallor and fatigue [11]. In other 25% of active cases, the infection moves from the lungs causing other kinds of TB, collectively denoted extra-pulmonary tuberculosis. This occurs more commonly in immunosuppressed persons and young children.

The main cause of tuberculosis, mycobacterium tuberculosis, is a small aerobic non-motile bacillus. High lipid content of this pathogen accounts for many its clinical characteristic. People with silicosis have an approximately 3-fold greater risk developing TB. People with chronic renal failure and also hemodialysis have a risk for developing TB than persons without diabetes mellitus. Low body weight is associated with the risk of TB.
Transmission can only occur from people with active-not-latent TB. The probability of transmission from one person to another depends upon the number of infections droplets expelled by a carrier, the effectiveness of ventilation, the duration of exposure and the virulence of the mycobacterium tuberculosis strain. The chains of transmission can be broken by isolating people with active disease and starting effective

anti tuberculosis therapy.

Tuberculosis prevention and control takes two parallel approaches. People with TB and their contacts are identified and then treated. Identification of infections often involves testing high-risk group for TB children are vaccinated to protect them from TB. No vaccine is available that provides reliable protection for adults [7].

2. Methodology

Mathematical model have played a vital role in the formulation of TB control strategies and the establishment of interim goal for intervention programme.

Our model is deterministic or compartmental SEI type model where the population is partitioned into classes based on the epidemiological state of individual and it is assumed that the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic. Hence, the TB transmissions dynamics between the compartments shall be described by a system of differential equation which shall be solved to obtain the disease free equilibrium state and the endemic equilibrium state. The stability analysis of the endemic equilibrium state shall be done using the reproduction number Ro while the disease free equilibrium state shall be earned out using the Routh-Hurwitz theorem.

2.1 Formulation of the Model

First, we define our variable, parameters and then state the assumption before we present the model.

Table 2.1: Description of Variables of the model

Variables	*Interpretation*
$S(t)$	The number of susceptible individual at time t.
$I(t)$	The number of infections individual at time t.
$E(t)$	The number of latently infected individual at time t.

Table 2.2: Description of Parameters of the model

Parameters	*Interpretation*
β	Contact rate (per person)
γ	Removal or infection rate (per People)
μ	Death rate=birth rate (per person)
μN	Birth rate
μS	Death rate (within susceptible population)
μI	Death rate (for the infective population)
σI	Disease rate
S/N	Susceptible fraction
I/N	Infective fraction
$\beta\frac{1}{N}S$	Incidence rate
I/β	Average contact period
I/γ	Average infection period
I/μ	Average death period
μE	Death rate (for the latent population)

The following assumptions are considered for the formulation or construction of the model

a. That all variable and rates are deterministic. That is, the value of any variable occurring in the model can be determined from its nature.

b. That the population size in a class is differentiable with respect to time. In other words, there is no up predictable change for any variable in the model.

c. That the population mixes homogeneously. That is, all susceptible individuals are equally likely to be infected by infections individuals in case of contact.

d. That people in each class have equal natural death rate of μ.

2.2 Model Description

Based on the SEI model, the population is partitioned into three classes namely: susceptible $S(t)$, Latent $E(t)$ and infection $I(t)$ classes. The susceptible class of the population increases due to fact that people are born into the population at the rate of μN and become infected at the rate of $\beta\frac{1}{N}S$. This component decreases due to the latent infection of individual at the rate $P\beta\frac{1}{N}S$ and due to death from natural causes at the rate of μS. The population of the latent class increases as a result of infection of individuals in the susceptible class at the rate of $P\beta\frac{1}{N}S$. This class reduces as a result of death from natural causes at the rate of μE. The infections class increase from the proportion of those who are latent carrier at the rate of $P\beta\frac{1}{N}S$ and γI due to delay in developing disease by some people in the latent class. This class reduces due to death from natural causes at the rate of μI and the disease at the rate of σI. The model can schematically be presented as shown below.

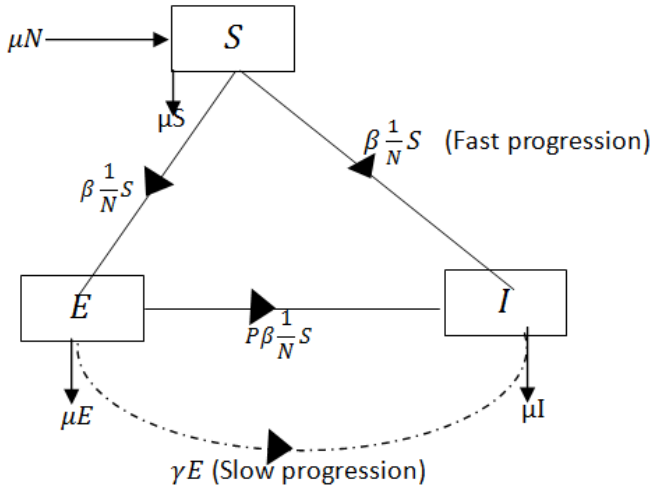

Figure 1: Schematic presentation of the model.

2.3 The Model Equations

Apply the assumption and the inter-relations between the variables, parameters and their meanings as described above, the mathematical model of Tuberculosis transmission

dynamics can be describe by the following differential equation.

$$\frac{dS}{dt} = \mu N - \left[\mu S + \beta \frac{1}{N} S\right]$$
$$= \mu N - \mu S - \beta \frac{1}{N} S \quad (2.1)$$

$$\frac{dE}{dt} = \beta \frac{1}{N} S - \left[(\gamma + \mu)E + P\beta \frac{1}{N} S\right]$$

$$= (1 - P)\beta \frac{1}{N} S - (\gamma + \mu)E \quad (2.2)$$

$$\frac{dI}{dt} = \beta \frac{1}{N} S(1 + P) + \gamma E - [\mu I + \sigma I]$$

$$= \beta \frac{1}{N} S(1 + P) + \gamma E - (\mu + \sigma)I \quad (2.3)$$

$$N(t) = S(t) + E(t) + I(t). \quad (2.4)$$

3. Stability Analysis of the model

In this section, the model is analyzed to investigate the state of the disease free equilibrium.

3.1 Analysis of the model equations

To make population non dimensional, we divide each side of each equation by N and set $s(t)\frac{S(t)}{N}, e(t) = \frac{E(t)}{N}, i(t) = \frac{I(t)}{N}$. Therefore in terms of the frequencies s, e *and* i, the system becomes

$$\frac{ds}{dt} = \mu - \mu s - \beta i s \quad (3.1)$$

$$\frac{de}{dt} = (1 - P)\beta i s - (\gamma + \mu)e \quad (3.2)$$

$$\frac{di}{dt} = \beta i s(1 + P) + \gamma e - (\mu + \sigma)i. \quad (3.3)$$

3.2 Steady State Solution

The steady state solution is often called the disease free equilibrium. The steady state infection gives the maximum number of susceptible who can be infected. Let $L(S, E, I)$ be the equilibrium point of the system described by the equation (3.1) – (3.3). At the equilibrium state, we have $\frac{ds}{dt} = \frac{de}{dt} = \frac{di}{dt} = 0$. That is

$$\mu - \mu s - \beta i s \quad (3.4)$$

$$(1 - P)\beta i s - (\gamma + \mu)e \quad (3.5)$$

$$\beta i s(1 + P) + \gamma e - (\mu + \sigma)i. \quad (3.6)$$

In order to obtain the disease free equilibrium state as well as the endemic equilibrium state, we solve equation (3.4) – (3.5) simultaneously. For the disease free equilibrium state, both latently infectious class and the infectious class must be zero, we have

$$\mu - \mu s_* - \beta i_* s_* = 0 \quad (3.7)$$

$$(1 - P)\beta i_* s_* - (\gamma + \mu)e_* \quad (3.8)$$

$$\beta i_* s_*(1 + P) + \gamma e_* - (\mu + \sigma)i_*. \quad (3.9)$$

Where s_* is the maximum number of susceptible, e_* is the maximum latent population and i_* is the maximum number of infected. From equation (3.8), we have

$$(1 - P)\beta i_* s_* = (\gamma + \mu)e_*$$
$$s_* = \frac{(\gamma+\mu)e_*}{(1-P)\beta i_*}. \quad (3.10)$$

From equation (3.8) and (3.9), we have

$$\beta i_* s_* = \frac{(\gamma+\mu)e_*}{1-P}$$
$$\beta i_* s_* = \frac{(\mu + \sigma)i_* - \gamma e_*}{1 + P}$$

Therefore

$$\frac{(\mu+\sigma)i_* - \gamma e_*}{1+P} = \frac{(\gamma+\mu)e_*}{1-P}$$
$$\frac{(\mu+\sigma)i_*}{1+P} = \left[\frac{\gamma}{1+P} + \frac{\mu+\gamma}{1-P}\right] e_*$$
$$= \frac{(1-P)\gamma+(1+P)(\mu+\gamma)e_*}{(1-P)(1+P)}$$
$$(\mu + \sigma)i_* = \frac{(\gamma - P\gamma + \mu + \gamma + P\mu + P\gamma)e_*}{1 - P}$$
$$= \frac{(2\gamma+(1+P)\mu)e_*}{1-P}$$
$$(1 - P)(\mu + \sigma)i_* = (2\gamma + (1 + P)\mu)e_*$$
$$\frac{e_*}{i_*} = \frac{(1-P)(\mu+\sigma)}{(2\gamma+(1+P)\mu)} \quad (3.11)$$

Substituting equation (3.11) into (3.10) gives

$$s_* = \frac{\mu+\gamma}{\beta(1-P)} \cdot \frac{(1-P)(\mu+\sigma)}{(2\gamma+(1+P)\mu)}$$

Therefore

$$s_* = \frac{(\mu+\gamma)(\mu+\sigma)}{\beta(2\gamma+(1+P)\mu)}.$$

3.3 Stability Analysis of the Disease-free Equilibrium State

To determine the stability or otherwise of the disease –free equilibrium state L_*, we examine the behavior of the model population near this equilibrium solution. We determine the condition(s) that must be met if the disease is to be totally eradicated from the population. We linearize equation (2.1), (2.2) and (2.3) to get the Jacobian matrix J

$$J = \begin{pmatrix} -\mu-\beta i & 0 & -\beta s \\ (1-P)\beta i & -\mu-\gamma & (1-P)\beta s \\ \beta i(1+P) & \gamma & \beta s(1+P)-(\mu+\sigma) \end{pmatrix}$$

At the disease –free equilibrium $L_*(s_*, e_*, i_*)$ the Jacobian matrix becomes

$$J_0 = \begin{pmatrix} -\mu & 0 & -\beta \\ 0 & -\mu-\gamma & (1-P)\beta \\ 0 & \gamma & \beta(1+P)-(\mu+\sigma) \end{pmatrix}$$

The characteristic equation $|J_0 - I\lambda| = 0$ is obtained from the Jacobian determinant with the eigen values $\lambda_i (i = 1,2,3)$

$$(J_0 - I\lambda) = \begin{vmatrix} -\mu-\lambda & 0 & -\beta \\ 0 & -\mu-\gamma-\lambda & (1-P)\beta \\ 0 & \gamma & \beta(1+P)-(\mu+\sigma)-\lambda \end{vmatrix} = 0$$

$(\mu+\lambda)[\gamma(1-P)\beta] + [(\lambda+\mu+\gamma)(\beta(1+P)) - (\mu+\sigma) - \lambda] = 0$

$\lambda_1 = -\mu$

$[\gamma(1-P)\beta] + [(\lambda+\mu+\gamma)(\beta(1+P)) - (\mu+\sigma) - \lambda] = 0$

$\Rightarrow \gamma\beta - P\gamma\beta + \lambda\beta + \lambda\beta P - \lambda\mu - \lambda\sigma - \lambda^2 + \beta\mu + \beta P\mu - \mu^2 + \sigma\mu - \mu\lambda + \gamma\beta + \gamma\beta P - \mu\gamma - \sigma\gamma - \lambda\gamma = 0$

$\Rightarrow \lambda^2 + \lambda(\beta + \beta P - \mu - \sigma - \mu - \gamma) + \beta\mu + \beta P\mu - \mu^2 + \sigma\mu + \gamma\beta + \gamma\beta P - \mu\gamma - \sigma\gamma - P\gamma\beta + \gamma\beta = 0$

$\Rightarrow \lambda^2 - \lambda(\beta + \beta P - 2\mu - \sigma - \gamma) + \mu^2 + \sigma\mu + \mu\gamma + \sigma\gamma - \beta\mu + \beta P\mu - \beta\gamma - \beta\gamma P - \gamma\beta + P\gamma\beta = 0$

Applying the formula method, we obtain $\lambda_{2,3} = \frac{\beta+\beta P-2\mu-\sigma-\gamma \pm \sqrt{(\beta+\beta P-2\mu-\sigma-\gamma)^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)}}{2}$

$= -\frac{(2\mu+\sigma+\gamma-\beta(1+P)) \pm \sqrt{(\beta(1+P)-2\mu-\sigma-\gamma)^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)}}{2}$

Hence

$\lambda_2 = -\frac{(2\mu+\sigma+\gamma-\beta(1+P)) - \sqrt{(\beta(1+P)-2\mu-\sigma-\gamma)^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)}}{2}$

$\lambda_3 = -\frac{(2\mu+\sigma+\gamma-\beta(1+P)) + \sqrt{(2\mu+\sigma+\gamma-\beta(1+P))^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)}}{2}$

If $2\mu+\sigma+\gamma-\beta(1+P)$ is positive and $-4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)$ is positive then λ_3 is less than zero if

$(2\mu+\sigma+\gamma-\beta(1+P)) + \sqrt{(2\mu+\sigma+\gamma-\beta(1+P))^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma)} < 0$

That is

$[(2\mu+\sigma+\gamma-\beta(1+P))]^2 - 4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma) < [(2\mu+\sigma+\gamma-\beta(1+P))]^2$

or

$$4(\mu^2+\sigma\mu+\mu\gamma-\beta\mu-\beta P\mu-2\beta\gamma+\sigma\gamma) > 0$$

$$\mu^2+\sigma\mu+\mu\gamma+\sigma\gamma-2\beta\gamma-(1+P)\beta\mu > 0$$

Therefore

$\mu(\mu+\sigma)+\gamma(\mu+\sigma) > \beta(2\gamma+(1+P)\mu).$

3.4 The Basic Reproduction Number R_0

The basic reproduction number R_0 is defined as the average number of secondary infections that occur when one infective is introduced into a completely susceptible host population [6]. $R_0 = \frac{1}{s_*}$. Hence

$$R_0 = \frac{1}{\frac{(\mu+\gamma)(\mu+\sigma)}{\beta(2\gamma+(1+P)\mu)}} \quad \frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)}. \qquad (3.12)$$

Therefore, the disease –free equilibrium state of the model is

$$L_*(s_* e_* i_*) = \frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)}.$$

4. Conclusion

In this paper, we present a mathematical model of Tuberculosis transmission dynamics. The population was partitioned into three compartments. The disease –free equilibrium state $L_*(s_* e_* i_*)$ was determined and its stability analysis conducted using the Routh Hurwitz theorem. The analysis shows that the necessary and sufficient condition for the disease equilibrium state to be stable is if $\frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)} < 1$ and unstable if $\frac{\beta(2\gamma+(1+P)\mu)}{(\mu+\gamma)(\mu+\sigma)} > 1$. This means that the disease may infect the whole population if we fail to control parameters $\beta, \gamma, P, \mu \text{ and } \sigma$ so that $R_0 < 1$.

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