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A MODEL FOR TRANSMISSION DYNAMICS OF TUBERCULOSIS WITH ENDEMIC EQUILIBRIUM

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ABSTRACT

In this paper, a mathematical model is proposed and analyzed to study the dynamics of tuberculosis based on MSEIR model. It is assumed that the rate at which number of latently infected individuals moves to recovery class R and again from recovery class to latent class L is not equal. The possibility of existence of endemic equilibrium state is discussed and examined the basic reproduction number.

Keywords: *Epidemiology, Latent TB Treatment, Transmission dynamics, Basic Reproduction Number, Endemic equilibrium state (Stability).*

AMS Subject Classification*: 92D30, 92D25, 34D20.*

1. INTRODUCTION

Tuberculosis, or TB, is an infectious bacterial disease caused by Mycobacterium tuberculosis (M. Tuberculosis), which most commonly affects the lungs. It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease. Tubercle bacilli carried by such droplets live in the air for a short period of time (about 2 hours), and therefore it is believed that occasional contact with an infectious case rarely leads to an infection. According to the World Health Organization (WHO), infants and young children infected with Mycobacterium tuberculosis are also more likely to develop active TB than older people since, their immune system are not yet well developed [7].

The Global burden of tuberculosis (TB) has increased over the past two decades despite widespread implementation of control measures including BCG vaccination and the World Health Organization's DOTS strategy which focuses on case finding and short-course chemotherapy [6]. The transmission dynamics of TB has received considerable attention for a long time, and different mathematical models have been developed incorporating various factors, such as fast and slow progression [2],treatment [3],drug-resistant strain [4], reinfection[11], coinfection with HIV[12], migration[15], chemoprophylaxis, relapse[10], exogenous reinfection [13], seasonality[9], and age dependent risk.

The spread of infectious diseases has always being concerns and a threat to public health. Tuberculosis which is deadly diseases on the rise and revisiting both developed and developing word. Globally it is the leading cause of death than any other infectious diseases like malaria, HIV, schistosomiasis, typhoid fever etc. In the study, compartment M in which all newborns have passive immunity, a latent compartment in which all the individuals have been affected but have not yet infectious. The next stage is the period of active TB infection when the individual start to exhibit some or all the symptoms of TB.

The structure of the paper is organized as; we formulate a simple ODE's model and prove the endemic equilibrium of the transmission dynamics of tuberculosis.

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2. METHODOLOGY

It is not unknown that mathematical modeling has had an important role in understanding of tuberculosis transmission dynamics. In our mathematical model one of the principal attribute of these models is that the force of infection (the rate at which susceptible leave the susceptible class and move into the infected category i.e. become infected) is a function of the number of infectious hosts in the population at any time t and is thus a non-linear term. Other transitions such as the recovery of infectious individuals and death are modeled as linear terms with constant coefficients. Therefore, the TB transmission dynamics between the compartments shall be described by a system of differential equation which shall be solved to obtain both the disease-free equilibrium state and the endemic equilibrium state. The stability analysis of the disease-free equilibrium state shall be carried out using the Routh- Hurwitz criterion while that of the endemic equilibrium state shall be done using the reproduction number, R_0.

2.1 ASSUMPTIONS OF THE MODEL

The model is based on the following assumptions.

1. That the population is heterogeneous. That is, the individuals that make up the population can be grouped into different compartments or groups according to their epidemiological state.
2. That the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic. In other words, that the changes in population of a compartment can be calculated using only history to develop the model.
3. That a proportion of the population of newborns is immunized against TB infection through vaccination.
4. That the immunity conferred on individuals by vaccination expires after some time at a given rate.
5. That the population mixes homogeneously. That is, all susceptible individuals are equally likely to be infected by infectious individuals in case of contact.
6. That the rate at which number of latently infected individuals moves to recovery class and again from recovery class to latent class is not equal.
7. That people in each compartment have equal natural death rate of μ.
8. That all newborns are previously uninfected by TB and therefore join either the immunized compartment or the susceptible compartment depending on whether they are vaccinated or not.
9. That there are no immigrants and emigrants. The only way of entry into the population is through new – born babies and the only way of exit is through death from natural causes or death from TB-related causes.

2.2 Formulation of Model:

We define our variable, parameter as

Table - 2.1: Description of variable of the model

Variables	Interpretation
M(t)	The number of individuals who are immunized against TB through vaccination at time t.
S(t)	The number of susceptible individual at time t.
L(t)	The number of latently infected individual at time t.
I(t)	The number of infective individuals at time t.
R(t)	The number of individuals who have been treated and have recovered from the infection at time t.
N(t)	The total population size.

Table - 2.2: Parameter of the model

Parameters	Interpretation
p	Population of new births joining the population.
θp	The proportion of new birth that have been immunized through vaccine.
α	The rate of expiration of vaccine efficiency.
μ	The natural death.
β	The rate at which susceptible individuals become latently infected by TB.

σ	The rate at which latently infected recover from TB through treatment.
τ	The rate at which latently infected become actively infected.
γ	The rate at which actively infected recover from TB infection.
π	The rate at which recovered individuals become latently infected individuals.
d	The tuberculosis death rate.

2.3 The Mathematical Model and Diagram:

The transmission dynamics of tuberculosis model can be described as in the compartment model in Fig. (1).

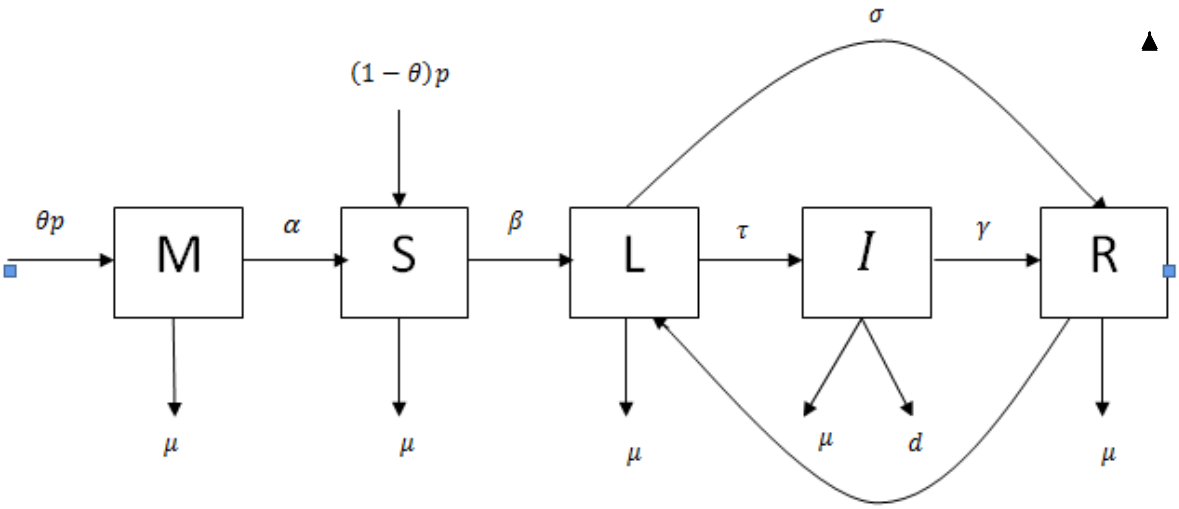

Fig. - (1): A compartmental diagram for transmission dynamics of tuberculosis

Model Equations:

In the view of above assumptions and their inter-relations between the variables and parameters as described in the compartmentalized model in Fig.(1), we have the following system of differential equations:

$$\frac{dM}{dt} = \theta p - (\alpha + \mu)M \tag{2.1}$$

$$\frac{dS}{dt} = (1-\theta)p + \alpha M - \beta SI - \mu S \tag{2.2}$$

$$\frac{dL}{dt} = \beta SI - (\alpha + \tau + \mu)L + \pi R \tag{2.3}$$

$$\frac{dI}{dt} = \tau L - (\gamma + \mu + d)I \tag{2.4}$$

$$\frac{dR}{dt} = \sigma L + \gamma I - (\mu + \pi)R \tag{2.5}$$

$$\therefore N(t) = M(t) + S(t) + L(t) + I(t) + R(t) \tag{2.6}$$

2.4 Equilibrium of the Model:

The governing system of equations of the model (2.1-2.6), we have E(M, S, L, I, R) be the equilibrium point. At the equilibrium state, we have

$$\frac{dM}{dt} = \frac{dS}{dt} = \frac{dL}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$$

That is,

$$\theta p - (\alpha + \mu)M = 0 \tag{2.7}$$

$$(1-\theta)p + \alpha M - \beta SI - \mu S = 0 \tag{2.8}$$

$$\beta SI - (\alpha + \tau + \mu)L + \pi R = 0 \tag{2.9}$$

$$\tau L - (\gamma + \mu + d)I = 0 \tag{2.10}$$

$$\sigma L + \gamma I - (\mu + \pi)R = 0 \tag{2.11}$$

2.5 The Endemic Equilibrium state:

The endemic equilibrium state is the state where the diseases cannot be totally eradicated but remains in the population. For the disease to persist in the population, immunized class, the infectious class and the recovered class must not be zero at equilibrium state. In other words, if $E^*(M^*, S^*, L^*, I^*, R^*)$ is the endemic equilibrium state, then $E^*(M^*, S^*, L^*, I^*, R^*) \neq (0,0,0,0,0)$ .In order to obtain the endemic equilibrium state, we solve equations [(2.7)-(2.11)] simultaneously taking into considering the fact $E^*(M^*, S^*, L^*, I^*, R^*) \neq (0,0,0,0,0)$.

From equation (2.7)

$$\theta p - (\alpha + \mu)M = 0$$

$$M^* = \frac{\theta p}{\alpha + \mu} \tag{2.12}$$

From Equation (2.10)
$\tau L - (\gamma + \mu + d)I = 0$

$$\Longrightarrow L = \frac{(\gamma + \mu + d)I}{\tau} \tag{2.13}$$

Substituting equation (2.13) into (2.9), we get

$$\beta SI - \frac{(\sigma + \tau + \mu)(\gamma + \mu + d)I}{\tau} + \pi R = 0$$

$$\Longrightarrow R = \frac{(\sigma + \tau + \mu)(\gamma + \mu + d)I - \beta SI\tau}{\tau\pi} \tag{2.14}$$

Substituting equation (2.13) for L and equation (2.14) for R in equation (2.11), we get

$\frac{\sigma(\gamma+\mu+d)I}{\tau} + \gamma I - \frac{(\mu+\pi)I}{\pi}\left[\frac{(\sigma+\tau+\mu)(\gamma+\mu+d)}{\tau} - \beta S\right] = 0$ (Since $I \neq 0$)

So,

$$\frac{\sigma(\gamma + \mu + d)}{\tau} + \gamma - \frac{(\mu + \pi)}{\pi}\left[\frac{(\sigma + \tau + \mu)(\gamma + \mu + d)}{\tau} - \beta S\right] = 0$$

$$\Longrightarrow S^* = \frac{\mu(\sigma + \tau + \mu)(\gamma + \mu + d) + \pi\tau(\mu + d) + \mu\pi(\gamma + \mu + d)}{\beta\tau(\mu + \pi)} \tag{2.15}$$

Substitute equation (2.12) from M and equation (2.15) for S in equation (2.8) gives

$$(1-\theta)p + \frac{\alpha\theta p}{(\alpha + \mu)} - (\beta I + \mu)S^* = 0$$

$$\Longrightarrow I = \frac{p(\alpha + \mu - \theta\mu)}{(\alpha + \mu)S^*\beta} - \frac{\mu}{\beta}$$

$$\Longrightarrow I^* = \frac{\beta p\tau(\alpha + \mu - \theta\mu)(\mu + \pi) - \mu(\alpha + \mu)[\mu(\gamma + \mu + d)(\pi + \sigma + \tau + \mu) + \pi\tau(\mu + d)]}{\beta(\alpha + \mu)[\mu(\gamma + \mu + d)(\pi + \sigma + \tau + \mu) + \pi\tau(\mu + d)]} \tag{2.16}$$

Substitute equation (2.16) for I in equation (2.13)

$$L = \frac{(\gamma + \mu + d)I^*}{\tau}$$

$$\Longrightarrow L^* = \frac{\beta p\tau(\alpha+\mu-\theta\mu)(\mu+\pi)(\gamma+\mu+d) - \mu(\alpha+\mu)(\gamma+\mu+d)[\mu(\gamma+\mu+d)(\pi+\sigma+\tau+\mu)+\pi\tau(\mu+d)]}{\tau\beta(\alpha+\mu)[\mu(\gamma+\mu+d)(\pi+\sigma+\tau+\mu)+\pi\tau(\mu+d)]} \tag{2.17}$$

By equation (2.11)
$\sigma L + \gamma I - (\mu+\pi)R = 0$

$$\Longrightarrow R = \left[\frac{\sigma(\gamma+\mu+d)+\gamma\tau}{\tau(\mu+\pi)}\right] I^*$$

$$\Longrightarrow R^* = \frac{[\sigma(\gamma+\mu+d)+\gamma\tau]\left[\beta p\tau(\alpha+\mu-\theta\mu)(\mu+\pi) - \mu(\alpha+\mu)[\mu(\gamma+\mu+d)(\pi+\sigma+\tau+\mu)+\pi\tau(\mu+d)]\right]}{\tau(\mu+\pi)\beta(\alpha+\mu)[\mu(\gamma+\mu+d)(\pi+\sigma+\tau+\mu)+\pi\tau(\mu+d)]} \tag{2.18}$$

Therefore the endemic equilibrium state is $E^*(M^*, S^*, L^*, I^*, R^*)$.

3. STABILITY ANALYSIS OF THE ENDEMIC EQUILIBRIUM STATE

The Jacobian Matrix of this model is

$$J = \begin{bmatrix} -(\alpha+\mu) & 0 & 0 & 0 & 0 \\ \alpha & -(\beta I+\mu) & 0 & -S\beta & 0 \\ 0 & \beta I & -(\sigma+\tau+\mu) & \beta S & \pi \\ 0 & 0 & \tau & -(\gamma+\mu+d) & 0 \\ 0 & 0 & \sigma & \gamma & -(\mu+\pi) \end{bmatrix}$$

At the endemic equilibrium state,E^* the Jacobian Matrix becomes

$$J^* = \begin{bmatrix} -(\alpha+\mu) & 0 & 0 & 0 & 0 \\ \alpha & -(\beta I^*+\mu) & 0 & -S^*\beta & 0 \\ 0 & \beta I^* & -(\sigma+\tau+\mu) & \beta S^* & \pi \\ 0 & 0 & \tau & -(\gamma+\mu+d) & 0 \\ 0 & 0 & \sigma & \gamma & -(\mu+\pi) \end{bmatrix}$$

The characteristics equation is $|J^* - I\lambda| = 0$

It is very difficult to find eigen values from the characteristics equation. We use basic reproduction number R_0 in analyzing the stability of the endemic equilibrium states. According to their work, when $R_0 > 1$, the system has a unique endemic equilibrium that is globally asymptotically stable. The same technique shall be adopted in this work to analysis the stability of the endemic equilibrium state

3.1 THE BASIC REPRODUCTION NUMBER, R_0

The basic reproduction number, R_0, as the average number of secondary infections caused by an infectious individual during his / her entire life as an infectious person.[5] Tuberculosis infection and re-infection are always existent in a community due to respiratory contact between the susceptible individuals, treated individuals, and the infectious individuals. Whether the disease becomes persistent or dies out depends on the magnitude of the basic reproductive number, R_0. Stability of equilibrium points can be analyzed using R_0. The disease-free equilibrium is locally asymptotically stable if $0< R_0 < 1$ and unstable if $R_0 >1$. In other words, when $0< R_0 < 1$, every infectious individual will cause less than one secondary infection and hence the disease will die out and when $R_0 > 1$, every infectious individual will cause more than one secondary infection and hence an epidemic will occur. All public health control measures are usually based on methods that, if effective, would lower R_0 to below unity.[14] .On the other hand, the endemic equilibrium is locally stable when $R_0 > 1$ and unstable when $0< R_0 < 1$.In order to control the spread of TB in any society effort must be made to ensure that the endemic equilibrium is unstable i.e. For the case of a single infected compartment, R_0 is simply the product of the infection rate and the mean duration of the infection**.** However, for more complicated models with several infected compartments, this simple definition of R_0 is insufficient. For a more general situation we can estimate this parameter by investigating the stability of the infection-free equilibrium [7] The expression for R_0 for Tuberculosis, which Blower [3], calculated from their simple model is given by:

$$R_0 = R_0^{Fast} + R_0^{Slow}$$

Where,

$$R_0^{Fast} = \left(\frac{\beta b}{\mu}\right)\left(\frac{1}{\mu+\mu_t}\right)\rho$$

$$R_0^{Slow} = \left(\frac{\beta b}{\mu}\right)\left(\frac{1}{\mu+\mu_t}\right)\left(\frac{(1-\rho)v}{v+\mu}\right)$$

In this model, it is assumed that the infected individuals can develop active TB by either direct progression (the disease develops immediately after infection) or endogenous reactivation (the disease develops after the infection). Because of these different ways of developing the disease, two types of TB must be modeled. These would be denoted as primary progressive TB (which is referred to as FAST Tuberculosis) and reactivation tuberculosis (which is referred to Slow tuberculosis)[1]. The expression for R_0 for TB, which Blower[3], calculated from their more detailed model is given as:

$$R_0 = R_0^{Fast} + R_0^{Slow} + R_0^{Relapse}$$

Where

$$R_0^{Fast} = \left(\frac{\beta b}{\mu}\right)\left(\frac{1}{\mu+\mu_0+c}\right)\rho f$$

$$R_0^{Slow} = \left(\frac{\beta b}{\mu}\right)\left(\frac{1}{\mu+\mu_t+c}\right)\left(\frac{q(1-\rho)v}{v+\mu}\right)$$

$$R_0^{Relapse} = \left(\frac{\beta b}{\mu}\right)\left[\frac{1}{(\mu+\mu_t+c)\left((\mu+\mu_t+c)-\left(\left(\frac{2wc}{2w+\mu}\right)\right)\right)}\right]\left[\left(p+\frac{(1-\rho)v}{v-\mu}\right)\left(\frac{wc}{2w+\mu}\right)\right]$$

These equations show that a Tuberculosis epidemic can be seen as a series of linked sub-epidemic [3]. The value of R_0 in each of the sub-epidemics is determined by the product of three components:

1. The average number of infections that one infectious case causes per unit time.
2. The average time that an individual remains infectious (which is the same for Fast and Slow TB but different for Relapse, and
3. The probability that a latent case will develop into an infectious case (which is different for Fast, Slow or Relapse TB) [1].

Ssematimba *et al*. [14] defined the reproduction number of tuberculosis in a density-dependent model as

$$R_0 = \left(\frac{\frac{\Lambda}{\mu}}{A}\right)\left(\frac{(\beta_1+\beta_2)c}{\mu+d+r_2}\right)\left(\frac{k}{\mu+k+r_1}\right)$$

Where,

$\left(\frac{\frac{\Lambda}{\mu}}{A}\right)$ is the density of the susceptible population.

β1c and β2c are the effective transmission rates.

$\left(\frac{1}{\mu+d+r_2}\right)$ is the effective infectious period.

$\left(\frac{(\beta_1+\beta_2)c}{\mu+d+r_2}\right)$ is the number of latent infections produced by a typical infectious individual during the mean infectious period.

$\left(\frac{k}{\mu+k+r_1}\right)$ is the probability of progression from latent stage into the infectious stage.

Taking this concept for our model, we have that R_0 is given by

$$R_0 = \left(\frac{(1-\theta)p+\alpha}{\mu+\beta}\right)\left(\frac{\beta+\pi}{\sigma+\mu+\tau}\right)\left(\frac{\tau}{\mu+d+\gamma}\right)$$

Where $\left(\frac{(1-\theta)p+\alpha}{\mu+\beta}\right)$ is the average number of individuals in the susceptible class.

$\left(\frac{\beta+\pi}{\sigma+\mu+\tau}\right)$ is the number of latent infectious produced by a typical infectious individual during the mean infectious period.

$\left(\frac{\tau}{\mu+d+\gamma}\right)$ is the probability of progressing from latent class into infectious class.

We must have $R_0 > 1$. That is

$$\left(\frac{(1-\theta)p+\alpha}{\mu+\beta}\right)\left(\frac{\beta+\pi}{\sigma+\mu+\tau}\right)\left(\frac{\tau}{\mu+d+\gamma}\right) > 1$$

$$\Rightarrow \frac{[(1-\theta)p+\alpha](\beta+\pi)\tau}{(\mu+\beta)(\mu+\tau+\sigma)(\mu+d+\gamma)} > 1$$

$$\Rightarrow [(1-\theta)p+\alpha](\beta+\pi)\tau > (\mu+\beta)(\mu+\tau+\sigma)(\mu+d+\gamma)$$

$$\Rightarrow \frac{[(1-\theta)p+\alpha](\beta+\pi)\tau}{(\mu+\beta)} > (\mu+\tau+\sigma)(\mu+d+\gamma)$$

The above inequality gives the necessary and sufficient condition for the endemic equilibrium state of the model to be globally asymptotically stable. The interpretation is that**,** for the endemic equilibrium state to be globally asymptotically stable, the product of total contraction and total breakdown of the Susceptible class given by $\frac{[(1-\theta)p+\alpha](\beta+\pi)\tau}{(\mu+\beta)}$ must be greater than the total removal rate from both the Latent and the Infectious classes given by $(\mu+\tau+\sigma)(\mu+d+\gamma)$ In order to control TB, we must ensure that $R_0 < 1$ (that is, the Endemic equilibrium state is never stable.)[8]

4. CONCLUSION

In this paper, the effect of vaccination and treatment on the transmission dynamics of Tuberculosis (TB) was analyzed. The Endemic equilibrium state of the model, using Basic reproduction number Ro shows that TB can effectively be controlled or even be eradicated if the total removal rate from both the latent and the infectious classes is always less than the product of total contraction and total breakdown of the susceptible class.

5. RECOMMENDATIONS:

The incidence of tuberculosis can greatly be minimized or possibly be eradicated in any population if effort is made to ensure that the endemic equilibrium of this model is never stable. This can be achieved if the following recommendations are considered.

1. There should be more enlightenment campaign on the dangers of TB and on its symptoms.
2. More effort should be made to encourage people to voluntarily go for TB tests by discouraging stigmatization of people infected by the disease.
3. TB tests and treatment should continue to be free-of-charge to enable poor people assess them.
4. People should be educated on the mode of transmission of the disease and on home-care strategies for people infected by the disease.

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