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A Mathematical Model of Tuberculosis Control Incorporating Vaccination, Latency and Infectious Treatments (Case Study of Nigeria)

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Abstract

In Nigeria, the National Tuberculosis and Leprosy Control Program concentrates only on Infectious Tuberculosis treatment leaving the Latently infected ones on the waiting list at the mercy of their immune system. In this research we modelled the effect of combining Immunization with Latent Tuberculosis treatment in controlling the spread of Tuberculosis. We established the existence of equilibrium states and analyzed the Disease free equilibrium state for stability using Routh-Hurwitz Theorem. The disease free equilibrium state (i.e.,

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the state of total eradication of Tuberculosis) will be stable if effort is intensified in bringing down both the contraction rate β and the rate of break down to Infectious Tuberculosis τ.

1 Introduction

Tuberculosis (TB) is a contagious bacterial infection caused by Mycobacterium tuberculosis. It usually affects the lungs (pulmonary tuberculosis). It can also affect the central nervous system, the lymphatic system, the brain, spine and the kidneys. Only people who have pulmonary TB are infectious. One-third of the world's population is currently infected with the TB bacillus and new infections are occurring at a rate of one per second [5].

Tuberculosis was among the top 10 causes of death worldwide in 2015 when 10.4 million people became ill from TB of which 1.8 million people died from TB including 400,000 with HIV + TB. Sixty percent of TB cases worldwide were concentrated in just six countries: China, India, Indonesia, Nigeria, Pakistan and South Africa [6].

Vaccination with Bacillus Calmatte-Guerine (BCG) at birth protects children from early infection of the disease, but the effect of these vaccines expires with time [2]. Hence detection and treatment of Latent Tuberculosis infections by administering Isoniazid Preventive Therapy prevents the breakdown of Latent Infections into Infectious cases; this, however, greatly reduces the rate of spread of the disease since only members of the Infectious class can spread the disease to others.

Dye [3] stated that the global leading causes of death from infectious diseases among adults are TB and HIV and the number of TB cases has risen significantly since the start of the HIV epidemic, particularly in Sub-Saharan Africa where the HIV epidemic is most severe.

2 Methodology

2.1 Model Equations

The population is partitioned into five Compartments namely, Immunized $M(t)$, Susceptible $S(t)$, Latently Infected $L(t)$, Infectious $I(t)$ and Recovered $R(t)$ Compartments. The model parameters are: Recruitment constant ρ, Proportion immunized at birth θ, Rate of weaning off of the vaccine α, Natural death rate μ, Tuberculosis contraction rate β, Successful cure of infectious Latent σ, Rate of Breakdown of Latent TB into Infectious TB τ, Successful cure of infectious TB patients γ and Death resulting from TB infection δ.

The model is represented by the following system of ordinary Differential Equations:

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

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

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

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

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

2.2 Model Diagram

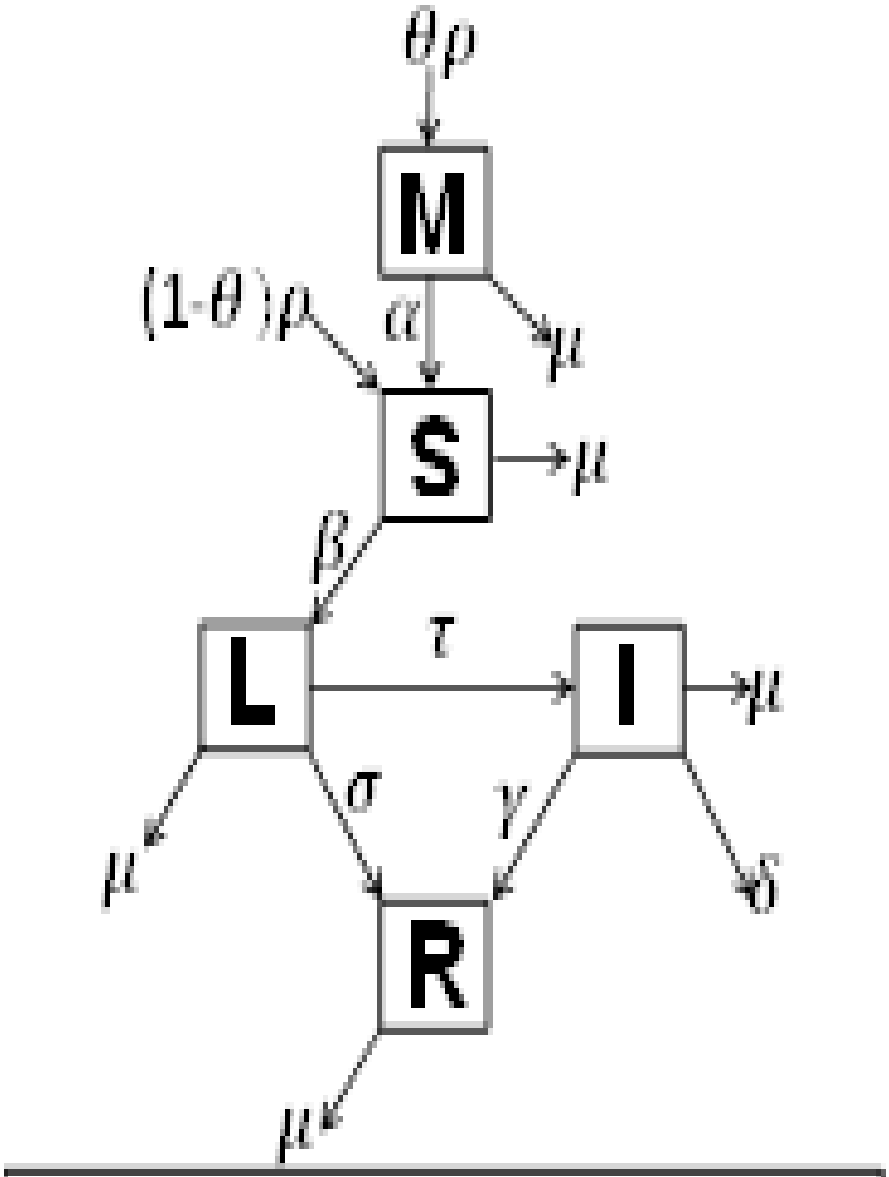

Figure 1: Schematic presentation of the model

3 Equilibrium Solutions

We now solve the model equations to obtain the equilibrium states.
At the equilibrium state $\frac{dM}{dt}=\frac{dS}{dt}=\frac{dL}{dt}=\frac{dI}{dt}=\frac{dR}{dt}=0$.
Let M (t) =v, S (t) = w, L (t) = x, I (t) = y and R (t) = z.
Then the system of equations becomes

$$\theta\rho - (\alpha+\mu)v = 0 \tag{3.6}$$

$$(1-\theta)\rho + \alpha v - w(\beta y + \mu) = 0 \tag{3.7}$$

$$\beta wy - (\sigma+\tau+\mu)x = 0 \tag{3.8}$$

$$\tau x - (\gamma+\mu+\delta)y = 0 \tag{3.9}$$

$$\sigma x + \gamma y - \mu z = 0 \tag{3.10}$$

Solving equations (3.6) to (3.10) simultaneously, we obtain:
$(v, w, x, y, z) = \left(\frac{\theta\rho}{(\alpha+\mu)}, \frac{(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho}{\mu(\alpha+\mu)}\ 0,\ 0,\ 0\right).$
as the disease free equilibrium state and

$$v = \frac{\theta\rho}{(\alpha+\mu)}$$

$$w = \frac{(\sigma+\tau+\mu)(\gamma+\mu+\delta)}{\beta\tau}$$

$$x = \frac{[\rho\beta\tau(\alpha+\mu) - \beta\tau\mu\theta\rho - \mu(\alpha+\mu)(\sigma+\tau+\mu)(\gamma+\mu+\delta)]\,(\gamma+\mu+\delta)}{\beta\tau(\alpha+\mu)\,[\mu(\gamma+\mu+\delta) + \tau(\mu+\delta) + [\sigma(\gamma+\mu+\delta) + \tau\gamma]]}$$

$$y = \frac{[\rho\beta\tau(\alpha+\mu) - \beta\tau\mu\theta\rho - \mu(\alpha+\mu)(\sigma+\tau+\mu)(\gamma+\mu+\delta)]\,\tau}{\beta\tau(\alpha+\mu)\,[\mu(\gamma+\mu+\delta) + \tau(\mu+\delta) + [\sigma(\gamma+\mu+\delta)+\tau\gamma]]}$$

$$z = \frac{[\rho\beta\tau(\alpha+\mu) - \beta\tau\mu\theta\rho - \mu(\alpha+\mu)(\sigma+\tau+\mu)(\gamma+\mu+\delta)]\,[\sigma(\gamma+\mu+\delta)+\tau\gamma]}{\mu\beta\tau(\alpha+\mu)\,[\mu(\gamma+\mu+\delta) + \tau(\mu+\delta) + [\sigma(\gamma+\mu+\delta)+\tau\gamma]]}$$

as the endemic equilibrium state.

4 Stability Analysis of Disease Free Equilibrium State

We now investigate the stability of the Disease free equilibrium state. To do this, we examine the behavior of the model population near the equilibrium state [6].

4.1 The Characteristic Equation

Recall that the system of equations in this model at equilibrium state is

$$\theta\rho - (\alpha+\mu)v = 0$$

$$(1-\theta)\rho + \alpha v - w(\beta y + \mu) = 0$$

$$\beta w y - (\sigma+\tau+\mu)x = 0$$

$$\tau x - (\gamma+\mu+\delta)y = 0$$

$$\sigma x + \gamma y - \mu z = 0.$$

The Jacobian matrix of this system of equations is given by

$$J_3 = \begin{pmatrix} -(\alpha+\mu) & 0 & 0 & 0 & 0 \\ \alpha & -(\beta y+\mu) & 0 & -\beta w & 0 \\ 0 & \beta y & -(\sigma+\tau+\mu) & \beta w & 0 \\ 0 & 0 & \tau & -(\gamma+\mu+\delta) & 0 \\ 0 & 0 & \sigma & \gamma & -\mu \end{pmatrix}.$$

The characteristic equation is obtained from the Jacobian determinant with the eigenvalues λ

$$\det(J_3 - \lambda I) =$$

$$\det \begin{pmatrix} -(\alpha+\mu+\lambda) & 0 & 0 & 0 & 0 \\ \alpha & -(\beta y+\mu+\lambda) & 0 & -\beta w & 0 \\ 0 & \beta y & -(\sigma+\tau+\mu+\lambda) & \beta w & 0 \\ 0 & 0 & \tau & -(\gamma+\mu+\delta+\lambda) & 0 \\ 0 & 0 & \sigma & \gamma & -(\mu+\lambda) \end{pmatrix} \tag{4.11}$$

$$= 0.$$

At the disease free equilibrium state

$$(v, w, x, y, z) = \left(\tfrac{\theta\rho}{(\alpha+\mu)}, \tfrac{(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho}{\mu(\alpha+\mu)},\ 0,\ 0,\ 0\right).$$

Hence, evaluating the determinant and substituting 0 for y in (4.11) give:

$$(\alpha+\mu+\lambda)(\mu+\lambda)\{-(\sigma+\tau+\mu+\lambda)(\gamma+\mu+\delta+\lambda)(\mu+\lambda)+\beta w\tau(\mu+\lambda)\} = 0.$$

$$\implies (\alpha+\mu+\lambda)(\mu+\lambda)^2\{-(\sigma+\tau+\mu+\lambda)(\gamma+\mu+\delta+\lambda)+\beta w\tau\} = 0.$$

$$\implies (\alpha+\mu+\lambda)(\mu+\lambda)^2\{(\sigma+\tau+\mu+\lambda)(\gamma+\mu+\delta+\lambda)-\beta w\tau\} = 0.$$

$$\implies (\alpha+\mu+\lambda)(\mu+\lambda)^2 \det \begin{pmatrix} -(\sigma+\tau+\mu+\lambda) & \beta w \\ \tau & -(\gamma+\mu+\delta+\lambda) \end{pmatrix} = 0. \tag{4.12}$$

From (4.12) either

$$(\alpha+\mu+\lambda)(\mu+\lambda)^2=0, \tag{4.13}$$

or

$$\det\begin{pmatrix} -(\sigma+\tau+\mu+\lambda) & \beta w \\ \tau & -(\gamma+\mu+\delta+\lambda) \end{pmatrix}=0. \tag{4.14}$$

From (4.13), $\lambda_1=\lambda_2=-\mu$ and $\lambda_3=-(\alpha+\mu)$.

To determine the nature of eigenvalues in (4.14), we present the Routh-Hurwitz necessary and sufficient conditions for all roots of the characteristic polynomial to have negative parts, thus implying asymptotic stability as applied by Sematimba [4] and Benya [1].

Lemma 4.3.1 (Routh-Hurwitz Conditions)

$$Let \quad J=\begin{pmatrix} f_x(x_*,y_*) & f_y(x_*,y_*) \\ g_x(x_*,y_* & g_y(x_*,y_* \end{pmatrix} \tag{4.15}$$

be the Jacobian matrix of the non-linear system

$$\left.\begin{array}{l} \frac{dx}{dt}=f(x,y) \\ \frac{dy}{dt}=g(x,y) \end{array}\right\} \tag{4.16}$$

evaluated at the critical point (x_*,y_*).

Then the critical point (x_*,y_*) :

1. is asymptotically stable if $trace(J)<0$ and $det(J)>0$,
2. is stable but not asymptotically stable if $trace(J)=0$ and $det(J)>0$,
3. is unstable if either, $trace(J)>0$ or $det(J)<0$.

Since $(\mathrm{v},\mathrm{w},\mathrm{x},\mathrm{y},\mathrm{z}) = \left[\frac{\theta\rho}{(\alpha+\mu)},\frac{(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho}{\mu(\alpha+\mu)},0,0,0\right]$ at the disease free equilibrium state, we now substitute $\frac{(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho}{\mu(\alpha+\mu)}$ for w in (4.14) to obtain

$$\det\begin{pmatrix} -(\sigma+\tau+\mu+\lambda) & \frac{\beta[(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho]}{\mu(\alpha+\mu)} \\ \tau & -(\gamma+\mu+\delta+\lambda) \end{pmatrix}=0. \tag{4.17}$$

$$\text{Let } A=\begin{pmatrix} -(\sigma+\tau+\mu) & \frac{\beta[(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho]}{\mu(\alpha+\mu)} \\ \tau & -(\gamma+\mu+\delta) \end{pmatrix}.$$

Then from matrix A we have

$$det(A)=(\sigma+\tau+\mu)(\gamma+\mu+\delta)-\tau\beta\left[\frac{[(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho]}{\mu(\alpha+\mu)}\right]$$

and $trace(A) = -(\sigma + \tau + \mu) - (\gamma + \mu + \delta)$. Clearly $trace(A) < 0$ since all the parameters are positive.

For the determinant of A to be > 0 we should have,

$$(\sigma + \tau + \mu)(\gamma + \mu + \delta) - \tau\beta \left[\frac{[(\alpha + \mu)(1 - \theta)\rho + \alpha\theta\rho]}{\mu(\alpha + \mu)} \right] > 0$$

$$(\sigma + \tau + \mu)(\gamma + \mu + \delta) > \tau\beta \left[\frac{[(\alpha + \mu)(1 - \theta)\rho + \alpha\theta\rho]}{\mu(\alpha + \mu)} \right]$$

4.2 Discussion of Result

From the stability analysis carried out in section four, the first three eigenvalues are all negative. We then established the necessary and sufficient conditions for all the roots of (4.14) to be negative using the Routh-Hurwitz theorem. The condition for the Disease Free Equilibrium State to be stable is that $(\sigma + \tau + \mu)(\gamma + \mu + \delta) > \tau\beta \left[\frac{[(\alpha+\mu)(1-\theta)\rho+\alpha\theta\rho]}{\mu(\alpha+\mu)} \right]$ which implies that the product of total contraction and total breakdown of Latent class should be less than the total removal rate from both Latent and Infectious classes.

4.3 Conclusion

In this study, we modeled the effect of combining Immunization with Latent Tuberculosis treatment in controlling the spread of Tuberculosis. The administration of BCG vaccines at birth protects children from early infection of the disease, but the effect of these vaccines expires with time. Hence detection and treatment of Latent Tuberculosis infections using Isoniazid Preventive Therapy prevents the breakdown of Latent Infections into Infectious cases, this however reduces greatly the rate of spread of the disease since only members of the Infectious class can spread the disease to others.

The disease free equilibrium state (i.e. the state of total eradication of Tuberculosis) will be stable if effort is intensified in bringing down both the contraction rate β and the rate of break down to Infectious Tuberculosis τ.

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