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Preventing Mother to Child Transmission of Tuberculosis Using Bacillus Calmette-Guérin Vaccine: A Deterministic Modelling Approach

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Abstract: The must critical stage in the development of a child is the infant stages because their immune system is not yet well developed. At this stage they can easily be infected with Mycobacterium tuberculosis and are also more likely to develop active TB than older people. In this study, we present a mathematical model of effect of bacillus calmette-guérin vaccine in preventing mother to child transmission of tuberculosis. We established the Disease free and the endemic equilibrium states and carried out the stability analysis of the Disease free equilibrium state (the state of complete eradication of Tuberculosis from the entire population). Tuberculosis can be eradicated completely if the total removal rate from the Infectious class is greater than the total number of latent infections produced throughout the infectious period. This can be achieved by effective immunization of new born infants against infection using BCG vacines.
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Key words: Bacillus calmette-guérin vaccine, disease free equilibrium state, stability and Immunity

INTRODUCTION

Tuberculosis (TB) is a contagious bacteria 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 (World Health Organization, 2007).

There are three major factors that determine the risk of becoming exposed to tubercle bacilli, they include the number of incident infectious cases in the community, the duration of infectiousness, and the number and nature of interactions between a case and a susceptible contact per unit of time of infectiousness Rieder (1999).

TB spreads from person to person through the air as a person with active tuberculosis coughs, sneezes, speaks, spits, or kisses. Note that not everyone infected with Mycobacterium tuberculosis becomes sick. After a person becomes infected, the tuberculosis bacteria are controlled by the person's immune system. When the bacteria spread out of control, the infection becomes active. A person can have active or latent (inactive) TB. Both active and latent TB are treatable and curable. Active TB means the bacteria are active in the body and they weaken the immune system. Only people with active TB can spread the disease. People with latent TB does not feel sick and do not have any symptoms. In some people, Mycobacterium tuberculosis remains inactive for a lifetime without becoming active while others are likely to develop active TB if their immune system is compromised by some deadly disease such as HIV. The early symptoms of active tuberculosis include: coughing up blood, weight loss, fever, loss of appetite, and also shortness of breath indicates an advanced stage of active tuberculosis.

TB progression from latent infection to active disease varies greatly. For instance, people with AIDS are more likely to develop to active TB after infection. A patient with AIDS who becomes infected with Mycobacterium tuberculosis has a 50% chance of developing active tuberculosis within 2 months and a 5 to 10% chance of developing active disease each year thereafter. 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 (Okyere, 2006).

Bacillus Calmette-Guérin (or Bacille Calmette-Guérin, BCG) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, *Mycobacterium bovis*, that has lost its virulence in humans by being specially cultured in an artificial medium for years. The bacilli have retained enough strong antigenicity to become a somewhat effective vaccine for the prevention of human tuberculosis. At best, the BCG vaccine is 80% effective in preventing tuberculosis for duration of 15 years; however,

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its protective effect appears to vary according to geography Colditz *et al*. (1995).

The air space between a mother and baby during breast feeding is so small to allow easy transmission of Tuberculosis from mother to child. In this work, we study the effect of Bacillus Calmette-Guérin vaccine in preventing Mother to child transmission of Tuberculosis using Mathematical Modelling technique. The model description, diagram and equations are presented in section two. We obtained the equilibrium states in section three while the stability analysis of the disease free equilibrium state was carried out in section four. The result was discussed in section five and concluding remarks presented in section six.

Model description: The population is partitioned into four compartments. A proportion θ of new births were given BCG vaccines at birth to protect them against infection. The Immunized compartment changes due to the coming in of the immunized children into the population where we assumed that a proportion θρ of the incoming individuals are immunized against infection. This compartment reduces due to expiration of duration of vaccine efficacy at the rate α and also by natural death at the rate μ.

The Susceptible population increases due to the coming in of new births not immunized against infection into the population at the rate (1-θ)ρ and the expiration of the efficacy of the vaccine at the rate α. The Susceptible population also diminishes due to natural death at rate μ and infection with an incident rate of infection β.

In the same way the population dynamic of the infectious class grows with the instantaneous incidence rate of infection β resulting from contacts of members of Susceptible class with Infectious class. This class also reduces by natural death rate μ, successful cure of infectious TB patients at the rate γ and death caused as result of chronic TB infection at the rate δ.

Lastly the dynamics of the Recovered class increases with successful cure of infectious TB patients at the rate γ and decreases by natural death rate μ.

Model diagram (Fig. 1):

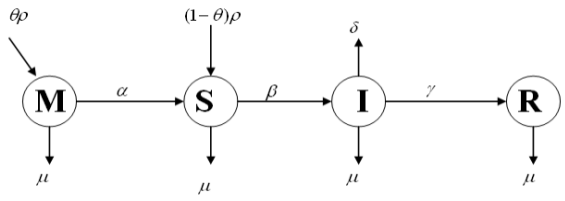

Fig. 1: Showing schematic presentation of the model

Model equations:

$$dM/dt = \theta\rho - (\alpha+\mu)M \quad (1)$$
$$dS/dt = (1-\theta)\rho + \alpha M - \beta SI - \mu S \quad (2)$$
$$dI/dt = \beta SI - (\gamma+\mu+\delta)I \quad (3)$$
$$dR/dt = \gamma I - \mu R \quad (4)$$

Equilibrium states of the model: We now solve the model equations to obtain the equilibrium states. At the equilibrium state:

$$dM/dt = dS/dt = dI/dt = dR/dt = 0$$

Let M(t) = w, S(t) = x, I(t) = y and R(t) = z

Then the system of equations become:

$$\theta\rho - (\alpha + \mu)\, w = 0 \quad (5)$$
$$(1 - \theta)\,\rho + \alpha w - x(\beta y + \mu) = 0 \quad (6)$$
$$y(\beta x - \gamma - \mu - \delta) = 0 \quad (7)$$
$$\gamma y - \mu z = 0 \quad (8)$$

The disease free equilibrium state:
From (7)

$$y(\beta x - \gamma - \mu - \delta) = 0$$
$$y = 0 \quad (9)$$

Or

$$\beta x - \gamma - \mu - \delta = 0 \quad (10)$$

Substituting (9) for y in (8) gives:

$$z = 0 \quad (11)$$

From (5)

$$w = \theta\rho / (\alpha + \mu) \quad (12)$$

Substituting (9) and (12) for y and w in (6) gives:

$$(1 - \theta)\rho + \alpha[\theta\rho / (\alpha + \mu)] - x(\beta y + \mu) = 0$$

$$\Rightarrow \quad x = \frac{\left[\alpha\rho + \mu(1-\theta)\rho\right]}{\mu(\alpha+\mu)} \quad (13)$$

Hence the disease free equilibrium state is:

$$(w,x,y,z) = \left(\frac{\theta\rho}{\alpha+\mu}, \frac{\left[\alpha\rho+\mu(1-\theta)\rho\right]}{\mu(\alpha+\mu)}, 0, 0\right)$$

The endemic equilibrium state:

From (10)

$$\beta x - \gamma - \mu - \delta = 0$$
$$x = (\gamma + \mu + \delta) / \beta \quad (14)$$

From (6)

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

$$y = \frac{(1-\theta)\rho + \alpha w - \mu x}{\beta x} \quad (15)$$

Substituting (12) and (14) for w and x in (15) gives:

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

$$y = \frac{(\alpha+\mu)\left[\beta\rho-(\gamma+\mu+\delta)\mu\right]-\beta\rho\mu\theta}{\beta(\alpha+\mu)(\gamma+\mu+\delta)} \quad (16)$$

Substituting (16) for y in (8) gives:

$$\gamma\left[\frac{(\alpha+\mu)\left[\beta\rho-(\gamma+\mu+\delta)\mu\right]-\beta\rho\mu\theta}{\beta(\alpha+\mu)(\gamma+\mu+\delta)}\right]-\mu z = 0$$

$$z = \left[\frac{\gamma(\alpha+\mu)\left[\beta\rho-(\gamma+\mu+\delta)\mu\right]-\beta\mu\theta\rho}{\beta\mu(\alpha+\mu)(\gamma+\mu+\delta)}\right] \quad (17)$$

Hence the endemic equilibrium state is given by:

$$w = \frac{\theta\rho}{(\alpha+\mu)}, x = \frac{\gamma+\mu+\delta}{\beta},$$

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

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

STABILITY ANALYSIS OF THE DISEASE FREE EQUILIBRIUM STATES

Having established the equilibrium states. We now investigate the stability of the Disease Free equilibrium states. To obtain this, we examine the behaviour of the model population near the equilibrium state Yusuf (2008).

The characteristic equation: Recall that the system of equations at equilibrium state is:

$$\theta\rho - (\alpha + \mu)w = 0$$
$$(1 - \theta)\rho + \alpha w - x(\beta y + \mu) = 0$$
$$y(\beta x - \gamma - \mu - \delta) = 0$$
$$\gamma y - \mu z = 0$$

We obtain the Jacobian matrix of this system of equations as presented by Benyah (2008):

$$J = \begin{pmatrix} -(\alpha+\mu) & 0 & 0 & 0 \\ \alpha & -(\beta y+\mu) & -\beta x & 0 \\ 0 & \beta y & (\beta x-\gamma-\mu-\delta) & 0 \\ 0 & 0 & \gamma & -\mu \end{pmatrix}$$

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

$$\det(J-\lambda I) = \det\begin{pmatrix} -(\alpha+\mu+\lambda) & 0 & 0 & 0 \\ \alpha & -(\beta y+\mu+\lambda) & -\beta x & 0 \\ 0 & \beta y & (\beta x-\gamma-\mu-\delta-\lambda) & 0 \\ 0 & 0 & \gamma & -(\mu+\lambda) \end{pmatrix} = 0$$

This gives:

$$-(\alpha+\mu+\lambda)\det\begin{pmatrix} -(\beta y+\mu+\lambda) & -\beta x & 0 \\ \beta y & (\beta x-\gamma-\mu-\delta-\lambda) & 0 \\ 0 & \gamma & -(\mu+\lambda) \end{pmatrix} = 0 \quad (18)$$

At the disease free equilibrium state:

$$(w,x,y,z) = \left(\frac{\theta\rho}{(\alpha+\mu)}, \frac{\left[\alpha\rho+\mu(1-\theta)\rho\right]}{\mu(\alpha+\mu)}, 0, 0\right)$$

Hence substituting 0 for y in (18) gives:

$$-(\alpha+\mu+\lambda)\det\begin{pmatrix}-(\mu+\lambda) & -\beta x & 0\\ 0 & (\beta x-\gamma-\mu-\delta-\lambda) & 0\\ 0 & \lambda & -(\mu+\lambda)\end{pmatrix}=0$$

Hence

$$-(\alpha+\mu+\lambda)\{-(\mu+\lambda)[-(\mu+\lambda)(\beta x-\gamma-\mu-\delta-\lambda)]\}=0$$

$$-(\alpha+\mu+\lambda)(\mu+\lambda)^2(\beta x-\gamma-\mu-\delta-\lambda)=0 \quad (19)$$

Substituting for x in (19) gives:

$$-(\alpha+\mu+\lambda)(\mu+\lambda)^2\left(\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}-\gamma-\mu-\delta-\lambda\right)=0$$

$$\Rightarrow -(\alpha+\mu+\lambda)(\mu+\lambda)^2=0 \quad (20)$$

Or

$$\left(\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}-(\gamma+\mu+\delta+\lambda)\right)=0 \quad (21)$$

From (20):

$$-(\mu+\lambda)^2=0$$

$$\lambda_1=\lambda_2=-\mu \quad (22)$$

and

$$\lambda_3=-(\alpha+\mu) \quad (23)$$

From (21):

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

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

$$\Rightarrow \lambda_4=\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}-(\gamma+\mu+\delta) \quad (24)$$

Note that λ_1, λ_2 and λ_3 are all negative; the disease free equilibrium state will be stable:

if $\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}<(\gamma+\mu+\delta)$

DISCUSSION

From the stability analysis carried out in section four above, the first three eigenvalues are negative. For the disease free equilibrium state (i.e., The state of complete eradication of Tuberculosis) to be stable, the fourth eigenvalue must also be negative, this is achieved when:

$$\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}<(\gamma+\mu+\delta)$$

where, $\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}$ is the number of latent infections produced and $(\gamma+\mu+\delta)$ is the total removal rate from the infectious class.

CONCLUSION

In this study we presented a mathematical model of effect of BCG vaccines in preventing Mother to Child transmission of Tuberculosis. The stability analysis carried out in section three above shows that the Disease free equilibrium state (i.e., The state of complete eradication of Tuberculosis) will be stable if:

$$\frac{\beta[\alpha\rho+\mu(1-\theta)\rho]}{\mu(\alpha+\mu)}<(\gamma+\mu+\delta)$$

meaning, The total removal rate from the Infectious class should be greater than the total number of latent infections produced throughout the infectious period.

It is however important to note here that for the population to be sustained the recovery rate from the infectious class γ must be greater than the natural death rate and the death rate due to infection combined together $\mu+\delta$ else the population will tend towards extinction.

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