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Post exposure vaccination for the dynamics of Tuberculosis with fast and slow latent period: A Mathematical model analysis

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Abstract: *In this paper we considered a nonlinear deterministic dynamical system to study the effect of post exposure vaccination on fast and slow latent infection stages. We found that there are two equilibrium points exist. These are disease free equilibrium point and endemic equilibrium point. Their local stability and global stability analysis investigated using nonlinear stability methods. We also found that the dynamical system has basic reproduction number* $R_0 = \frac{p\omega\beta_1\Lambda(\varepsilon+\epsilon+d)[\alpha(\theta+d)+\rho\theta]+(1-p)\omega\beta_1\Lambda(\rho+\alpha+d)[\epsilon(\theta+d)+\theta\varepsilon]}{dN(\omega+d)(\rho+\alpha+d)(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$ *it depends on thirteen parameters. Using the collected standard data we found the numerical value of the reproduction number is* $R_0 = 1.6684 > 1$. *This shows that the considered disease spreads in the community. From the sensitivity index of the model we found that the most sensitive parameter is the effective contact rate* β_1. *From numerical simulation, we observe that the recovery rate from fast latent by post exposure vaccination* ρ *, recovery rate from slow latent by post exposure vaccination* ε *, the recurrence rate* θ *and the effective contact rate* β_1 *are influencing the basic reproduction number.*

Keywords: *Nonlinear dynamical system, TB Post exposure vaccination, Stability analysis, Numerical simulation, Sensitivity analysis.*

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I. Introduction

Tuberculosis is a preventable and curable disease caused by slowly replicating Mycobacterium tuberculosis. This Mycobacterium tuberculosis often affects the lungs and any part of the body such as the kidney, spine, and brain. Tuberculosis claims the second largest number of victims due to a single infectious agent next to HIV/AIDS [20, 17, 3]. Mycobacterium tuberculosis is the cause of most occurrences of tuberculosis (TB) and is usually acquired via airborne infection from someone who has active TB can coughs, sneezes, speaks, or sings. German Microbiologist Robert Koch discovered the causative organism Mycobacterium tuberculosis on 24th March 1882 [14]. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB) [18].Tuberculosis is an ancient and complex infectious disease on which a large number of theoretical studies have been carried out. Mycobacterium tuberculosis infection can remain latent, become active, or it can progress from latent TB to active TB either by endogenous re-activation and/or exogenous re-infection. According to the World Health Organization, one-third of the world's population is infected, either latently or actively with tuberculosis [21].

Mathematical Modeling has become a powerful tool for analysing epidemiological characteristics [6, 11, 19, 8, 10]. Different mathematical models have been developed for defining target sub-populations for treating latent and active TB infections and incorporating certain factors, such as drug-resistant strains, co-infection with HIV, relapse, re-infection and vaccination to study the transmission dynamics of TB. In particular, Bhunuet et al. [1] considered a TB model incorporated the treatment of infectives and chemoprophylaxis. Liu et al. [12] studied a TB model incorporating seasonality. [22] Studied the Analysis of Transmission and Control of Tuberculosis in Mainland China, 2005–2016, Based on the Age-Structure Mathematical Model. Bowong et al. [2] considered Modeling and analysis of the transmission dynamics of tuberculosis without and with seasonality. [23] Addressed Modeling and stability analysis for a tuberculosis model with healthy education and treatment. [9] Proposed a multi-group SEIRV dynamical model with bidirectional mixed cross infection between cattle and sheep, and aim to investigate the influence of cross infection of mixed feeding on the brucellosis transmission. [7] Addressed What Dose a Mathematical Model tells About the Impact of Reinfection in Korean Tuberculosis Infection. [15] Studied on the dynamics of a Mathematical Model for Tuberculosis with variability in Susceptibility and Disease progressions due to difference in awareness level. [13] Addressed Liapunov Functions for Tuberculosis Models with Fast and Slow Progression. [16] Studied on the analysis of a mathematical model for tuberculosis: that could enhance the case detection rate of tuberculosis. [5] Propose a Mmathematical Model

to Predict the Prevalence and Transmission Dynamics of Tuberculosis in Amansie West District, Ghana. [3] Propose discrete age-structured SEIT model with application to tuberculosis transmission in China. In this paper, we will only consider the effect of post exposer vaccination. Hence, we will introduce and analyze a mathematical model for the transmission of TB with post exposer vaccination at slow and fast latent.

The Mathematical Model

In this paper we extend the work done by [19] by adding two assumptions that including the exposed compartment between susceptible and latent infected class and splitting the latent infected class in to slow latent and fast latent infected classes.

Model assumptions

Consider a nonlinear dynamical system in which the host population sub divides into six mutually-exclusive compartments, Tuberculosis susceptible individuals $S(t)$, TB-exposed individuals $E_T(t)$, TB-fast latently infected individuals $L_f(t)$, TB-slow latently infected individuals $L_s(t)$, active TB infected individuals $I_T(t)$ and TB recovered/treated individuals $R(t)$. The total population at time t, denoted by $N(t)$, is given by $N(t) = S(t) + E_T(t) + L_f(t) + L_s(t) + I_T(t) + R(t)$. We assume that all individuals in a given compartment are identically infectious, which might ignore potential effects caused due to variation among individuals. The susceptible class, $S(t)$, comprising individuals at risk of TB.The susceptible population is increased by the recruitment of individuals into the population at a rate Λ. All individuals in different compartments suffer from natural death rate d. Susceptible individuals acquire TB infection from individuals with active TB at a rate λ_T given by $\lambda_T = \frac{\beta_1}{N} I_T(t)$, where β_1 is the effective contact rate for TB infection.
TB-exposed individuals are progress to either fast or slow latent infection by the rate $p\omega$ and $(1-p)\omega$ respactivly. The fast latent $L_f(t)$and slow latent $L_s(t)$infected classes are decreased by post exposure vaccination by the linear recovery rate ρ and ε respectivly and inters into recovered class and if not get post exposure vaccination develop active TB infection at some time in the time of infection by the infection rate α and ϵ respectively and inter into $I(t)$. Individuals with active TB disease suffering induced death at a rate d_T. Individuals successfully treated at active TB infection stage develop immunity and go to recovery stage at a rate π.The recovered class are decrease by the rate θ which is the recurrence rate of successfully treated TB cases and inters into infected class. Based on the above assumptions we construct the following flow chart

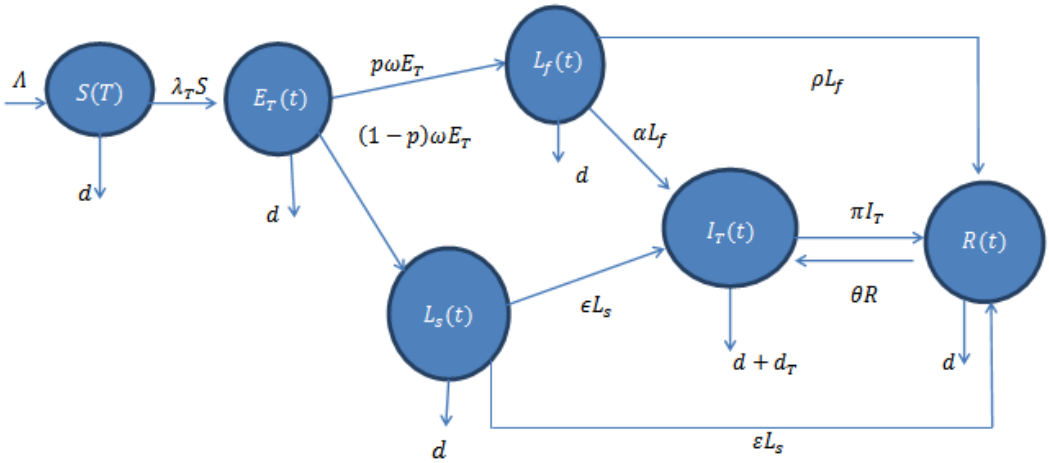

Figure1: Flow diagram for Tuberculosis dynamics

The corresponding dynamical system of the above flowchart is

$$\frac{dS}{dt} = \Lambda - \lambda_T S - dS \quad (1)$$

$$\frac{dE_T}{dt} = \lambda_T S - (\omega + d)E_T \quad (2)$$

$$\frac{dL_f}{dt} = p\omega E_T - (\rho + \alpha + d)L_f \quad (3)$$

$$\frac{dL_s}{dt} = (1-p)\omega E_T - (\varepsilon + \epsilon + d)L_s \quad (4)$$

$$\frac{dI_T}{dt} = \alpha L_f + \epsilon L_s + \theta R - (\pi + d + d_T)I_T \quad (5)$$

$$\frac{dR}{dt} = \rho L_f + \varepsilon L_s + \pi I_T - (\theta + d)R \quad (6)$$

Where,

$\lambda_T = \frac{\beta_1}{N} I_T(t)$ and, now, $N = S + E_T + L_f + L_s + I_T + R$

Positivity of solutions of the dynamical system (1) - (6)

Theorem

If $S(0) > 0, E_T(0) \geq 0, L_f(0) \geq 0, L_s(0) \geq 0,\ I_T(0) \geq 0\ and\ R(0) \geq 0$ then the solution region $\{S(t), E_T(t), L_f(t), L_s(t), I_T(t), R(t)\}$ of the dynamical system (1)-(6) is positive for all time t $\geq$ 0

Proof

To show this we have taken each differential equation of the dynamical system (1) - (6) is positive

1) From $\frac{dS}{dt} = \Lambda - \lambda_T S - dS$ its solution is $S(t) = e^{\int_0^t (\lambda_T + d)d\tau} \int_0^t \Lambda e^{-\int_0^t (\lambda_T + d)d\tau} d\tau > 0$ since those model parameters and exponential functions are positive.

2) From $\frac{dE_T}{dt} = \lambda_T S - (\omega + d)E_T$ its solution is $E_T(t) = e^{\int_0^t (\omega + d)d\tau} \int_0^t \lambda_T S e^{-\int_0^t (\omega + d)d\tau} d\tau > 0$ since those model parameters and exponential function is positive.

3) From $\frac{dL_f}{dt} = p\omega E_T - (\rho + \alpha + d)L_f$ its solution is $L_f(t) = e^{\int_0^t (\rho + \alpha + d)d\tau} \int_0^t p\omega E_T e^{-\int_0^t (\rho + \alpha + d)d\tau} d\tau > 0$ since those model parameters and exponential functions are positive.

4) From $\frac{dL_s}{dt} = (1 - p)\omega E_T - (\varepsilon + \epsilon + d)L_s$ its solution is $L_s(t) = e^{\int_0^t (\varepsilon + \epsilon + d)d\tau} \int_0^t (1 - p)\omega E_T e^{-\int_0^t (\varepsilon + \epsilon + d)d\tau} d\tau > 0$ since those model parameters and exponential function are positive.

5) From $\frac{dI_T}{dt} = \alpha L_f + \epsilon L_s + \theta R - (\pi + d + d_T)I_T$ its solution is $L_s(t) = e^{\int_0^t (\pi + d + d_T)d\tau} \int_0^t (\alpha L_f + \epsilon L_s + \theta R) e^{-\int_0^t (\pi + d + d_T)d\tau} d\tau > 0$ since those model parameters and exponential function is positive.

6) From $\frac{dR}{dt} = \rho L_f + \varepsilon L_s + \pi I_T - (\theta + d)R$ its solution is $R(t) = e^{\int_0^t (\theta + d)d\tau} \int_0^t (\rho L_f + \varepsilon L_s + \pi IT) e{-}0t\theta{+}dd\tau d\tau{>}0$ since those model parameters and exponential function are positive.

Boundedness of solutions of the dynamical system (1) - (6)

Theorem

If $\Omega_1 = \{(S, E_T, L_f, L_s, I_T, R) \in \mathbb{R}_+^6 : S(t) + E_T(t) + L_f(t) + L_s(t) + I_T(t) + R(t)\}$ is the feasible region of dynamical system (1) – (6) and then the solution of the dynamical system (1) – (6) $(S(t), E_T(t), L_f(t), L_s(t), I_T(t), R(t)) \in \Omega_1$ for all $t \geq 0$

Proof

The total population in our model is denoted by N and thus we do have $N(t) = S(t) + E_T(t) + L_f(t) + L_s(t) + I_T(t) + R(t)$. And thus $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE_T}{dt} + \frac{dL_f}{dt} + \frac{dL_s}{dt} + \frac{dI_T}{dt} + \frac{dR}{dt}$.

That is $\frac{dN}{dt} = \Lambda - dN - d_T I_T \leq \Lambda - dN$. After some calculation we get $N(t) \leq \frac{1}{d}(\Lambda - e^{\frac{-1}{d}(t+c)})$, for any constant $c = -d \ln(\Lambda - \mathrm{d}N_0)$ at an initial point $N(0) = N_0 . \Longrightarrow\ N(t) \leq \frac{\Lambda}{d}\left(1 - e^{\frac{-t}{d}}\right) + N_0 e^{\frac{-t}{d}}$. This shows that all solutions in Ω_1 remain in Ω_1 for all time $t \geq 0$.

Disease free equilibrium point

The disease free equilibrium point is obtained by setting the right-hand sides of the dynamical system (1) – (6) equal to zero with assumption $I_T = 0$ and we obtain $E_0 = (\frac{\Lambda}{d}, 0,0,0,0,0)$.

Basic Reproduction Number R_0

The basic reproduction number R_0 is defined as the effective number of secondary infections produced by a single infectious individual introduced in a wholly susceptible population during his or her entire infectious period [4]. This definition is given for the models that represent spread of infection in a population. We calculate the basic reproduction number by using the next generation operator method on the dynamical system (1) – (6). In the dynamical system (1) – (6) the rate of appearance of new infections $\mathcal{F}$ and the transfer rate of individuals $\mathcal{V}$ at the disease free steady state $E_0 = (\frac{\Lambda}{d}, 0,0,0,0,0)$ is

$$\mathcal{F}=\begin{pmatrix}0&0&0&\frac{\beta_1\Lambda}{dN}&0\\0&0&0&0&0\\0&0&0&0&0\\0&0&0&0&0\end{pmatrix},\qquad V=\begin{pmatrix}\omega+d&0&0&0&0\\-p\omega&\rho+\alpha+d&0&0&0\\-(1-p)\omega&0&\varepsilon+\epsilon+d&0&0\\0&-\alpha&-\epsilon&\pi+d+d_T&-\theta\\0&-\rho&-\varepsilon&-\pi&\theta+d\end{pmatrix}$$

and $V^{-1}=\begin{pmatrix}\frac{1}{\omega+d}&0&0&0&0\\\frac{p\omega}{(\omega+d)(\rho+\alpha+d)}&\frac{1}{\rho+\alpha+d}&0&0&0\\\frac{(1-p)\omega}{(\omega+d)(\varepsilon+\epsilon+d)}&0&\frac{1}{\varepsilon+\epsilon+d}&0&0\\m_1&m_2&m_3&m_4&m_5\\m_6&m_7&m_8&m_9&m_{10}\end{pmatrix}$. Where

$m_1=\frac{p\omega[\alpha(\omega+d)+\rho\theta]}{(\omega+d)(\rho+\alpha+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}+\frac{(1-p)\omega[\epsilon(\theta+d)+\theta\varepsilon]}{(\omega+d)(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$ $m_2=\frac{\alpha(\theta+d)+\rho\theta}{(\rho+\alpha+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$,
$m_3=\frac{\epsilon(\theta+d)+\theta\varepsilon}{(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$, $m_4=\frac{(\theta+d)}{(\pi+d+d_T)(\theta+d)-\theta\pi}$,
$m_5=\frac{\theta}{(\pi+d+d_T)(\theta+d)-\theta\pi}$, $m_6=\frac{p\omega[\alpha\pi-\rho(\pi+d+d_T)]}{(\omega+d)(\rho+\alpha+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}+\frac{(1-p)\omega[\epsilon\pi-\varepsilon(\pi+d+d_T)]}{(\omega+d)(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$ $m_7=\frac{\alpha\pi-\rho(\pi+d+d_T)}{(\rho+\alpha+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$, $m_8=\frac{\epsilon\pi-\varepsilon(\pi+d+d_T)}{(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$, $m_9=\frac{\pi}{(\pi+d+d_T)(\theta+d)-\theta\pi}$ and $m_{10}=\frac{\pi+d+d_T}{(\pi+d+d_T)(\theta+d)-\theta\pi}$. The spectral radius or Eigen value of FV^- is the required basic reproduction number obtained by

$R_0=\frac{p\omega\beta_1\Lambda(\varepsilon+\epsilon+d)[\alpha(\theta+d)+\rho\theta]+(1-p)\omega\beta_1\Lambda(\rho+\alpha+d)[\epsilon(\theta+d)+\theta\varepsilon]}{dN(\omega+d)(\rho+\alpha+d)(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$.

Local Stability of the Disease Free Equilibrium E_0

Theorem

The disease free equilibrium point $E_0=(\frac{\Lambda}{d},0,0,0,0,0)$ of the dynamical system (1)-(6) is locally asymptotically stable if $R_0<1$ whereas unstable if $R_0>1$.

Proof

The Jacobean matrix of the dynamical system (1) - (6) at the DFE point$E_0=(\frac{\Lambda}{d},0,0,0,0,0)$ is:

$$J(E_0)=\begin{pmatrix}-d&0&0&0&-\frac{\beta_1\Lambda}{dN}&0\\0&-(\omega+d)&0&0&\frac{\beta_1\Lambda}{dN}&0\\0&p\omega&-(\rho+\alpha+d)&0&0&0\\0&(1-p)\omega&0&-(\varepsilon+\epsilon+d)&0&0\\0&0&\alpha&\epsilon&-(\pi+d+d_T)&\theta\\0&0&\rho&\varepsilon&\pi&-(\theta+d)\end{pmatrix}$$

The corresponding characteristic equation of the above Jacobian matrix is

$$\begin{vmatrix}-d-\lambda&0&0&0&-\frac{\beta_1\Lambda}{dN}&0\\0&-(\omega+d)-\lambda&0&0&\frac{\beta_1\Lambda}{dN}&0\\0&p\omega&-(\rho+\alpha+d)-\lambda&0&0&0\\0&(1-p)\omega&0&-(\varepsilon+\epsilon+d)-\lambda&0&0\\0&0&\alpha&\epsilon&-(\pi+d+d_T)-\lambda&\theta\\0&0&\rho&\varepsilon&\pi&-(\theta+d)-\lambda\end{vmatrix}=0$$

After some calculations and using Routh Hurwitz stability criteria we get all the root of the characteristics equation are negative if $R_0<1$ and some of the eigenvalues are positive if $R_0>1$. Therefore the disease free equilibrium point is stable if $R_0<1$ and unstable if $R_0>1$.

Global stability of the disease free equilibrium E_0

Theorem

The disease-free equilibrium $\boldsymbol{E_0}=(\frac{\boldsymbol{\Lambda}}{\boldsymbol{d}},\mathbf{0},\mathbf{0},\mathbf{0},\mathbf{0},\mathbf{0},)$ is globally asymptotically stable if

$\frac{(S-S^*)\Lambda}{S}+\frac{p\omega\beta_1 I_T S}{N(\omega+d)}+\frac{\alpha p\omega E_T}{(\rho+\alpha+d)}+\frac{\epsilon(1-p)\omega E_T}{(\varepsilon+\epsilon+d)}+\frac{\pi(\alpha L_f+\epsilon L_s+\theta R)}{(\pi+d+d_T)}+\frac{\theta(\rho L_f+\varepsilon L_s+\pi I_T)}{(\theta+d)}>\frac{\beta_1 I_T(S-S^*)}{N}+d(S-S^*)+p\omega E_T+\alpha L_f+\epsilon L_s+\pi I_T+\theta R$

Proof

We define the Liapunov function $L: R_+^6\to R_+$ by:

$L(\mathbf{S}, \boldsymbol{E_T}, \boldsymbol{L_f}, \boldsymbol{L_s}, \boldsymbol{I_T}, \boldsymbol{R}) = \boldsymbol{u_1}\left(\boldsymbol{S} - \mathbf{S(0)} - \mathbf{S(0)}\ln\frac{\mathbf{S}}{\mathbf{S(0)}}\right) + \boldsymbol{u_2}\frac{\boldsymbol{p\omega}}{(\boldsymbol{\omega}+\boldsymbol{d})}\boldsymbol{E_T} + \boldsymbol{u_3}\frac{\boldsymbol{\alpha}}{(\boldsymbol{\rho}+\boldsymbol{\alpha}+\boldsymbol{d})}\boldsymbol{L_f} + \boldsymbol{u_4}\frac{\boldsymbol{\epsilon}}{(\boldsymbol{\varepsilon}+\boldsymbol{\epsilon}+\boldsymbol{d})}\boldsymbol{L_s} + \boldsymbol{u_5}\frac{\boldsymbol{\pi}}{(\boldsymbol{\pi}+\boldsymbol{d}+\boldsymbol{d_T})}\boldsymbol{I_T} + \boldsymbol{u_6}\frac{\boldsymbol{\theta}}{(\boldsymbol{\theta}+\boldsymbol{d})}\boldsymbol{R}$, and thus we get L is continuous function for all $(S, E_T, L_f, L_s, I_T, R) \in \Re_+^6$ and has 1st order partial derivatives and L has minimum at $(S(0), E_T(0), L_f(0), L_s(0), I_T(0), R(0)) = (\frac{\Lambda}{d}, 0,0,0,0,0)$, which is $L(\frac{\Lambda}{d}, 0,0,0,0,0) = 0$. Finally we calculate the time derivative of $L(\mathrm{S}, E_T, L_f, L_s, I_T, R)$ along the solution path yields

$\frac{\boldsymbol{dL(S,E_T,L_f,L_s,I_T,R)}}{\boldsymbol{dt}} = \boldsymbol{L_1} - \mathbf{L_2}$ **Where,** $\boldsymbol{L_1} = \frac{(\boldsymbol{S}-\mathbf{S}^*)\boldsymbol{\Lambda}}{\boldsymbol{S}} + \frac{\boldsymbol{p\omega\beta_1 I_T S}}{\boldsymbol{N(\omega+d)}} + \frac{\boldsymbol{\alpha p\omega E_T}}{\boldsymbol{(\rho+\alpha+d)}} + \frac{\boldsymbol{\epsilon(1-p)\omega E_T}}{\boldsymbol{(\varepsilon+\epsilon+d)}} + \frac{\boldsymbol{\pi(\alpha L_f+\epsilon L_s+\theta R)}}{\boldsymbol{(\pi+d+d_T)}} + \frac{\boldsymbol{\theta(\rho L_f+\varepsilon L_s+\pi I_T)}}{\boldsymbol{(\theta+d)}} > 0$

And $\mathbf{L_2} = \frac{\boldsymbol{\beta_1 I_T(S-\mathbf{S}^*)}}{\boldsymbol{N}} + \boldsymbol{d}(\boldsymbol{S} - \mathbf{S}^*) + \boldsymbol{p\omega E_T} + \boldsymbol{\alpha L_f} + \boldsymbol{\epsilon L_s} + \boldsymbol{\pi I_T} + \boldsymbol{\theta R} > 0$. **Therefore we conclude that if** $\boldsymbol{L_1} < \mathbf{L_2}$ **then,** $\frac{\boldsymbol{dL(S,E_T,L_f,L_s,I_T,R)}}{\boldsymbol{dt}} < 0$**,** which implies the disease free equilibrium point is globally asymptotically stable.

Endemic Equilibrium point E^*

Endemic equilibrium point is steady-state solutions where the disease persists in the population and is obtained by setting the right hand side of the dynamical system (1)-(6) equal to zero. Thus we get the endemic equilibrium point is

$$E^* = \left\{ \begin{matrix} \frac{\Lambda}{dR_0}, \frac{\Lambda}{(\omega+d)}\left(1-\frac{1}{R_0}\right), \frac{p\omega\Lambda}{(\omega+d)(\rho+\alpha+d)}\left(1-\frac{1}{R_0}\right), \frac{(1-p)\omega\Lambda}{(\omega+d)(\varepsilon+\epsilon+d)}\left(1-\frac{1}{R_0}\right), \\ \frac{dNR_0}{\beta_1}\left(1-\frac{1}{R_0}\right), \frac{\Lambda}{(\omega+d)}\left[\frac{p\omega\Lambda}{(\omega+d)(\rho+\alpha+d)} + \frac{(1-p)\omega\Lambda}{(\omega+d)(\varepsilon+\epsilon+d)} + \frac{\pi dN}{\beta_1\Lambda}R_0\right]\left(1-\frac{1}{R_0}\right) \end{matrix} \right\}$$

Local stability of the endemic equilibrium

Theorem

If $R_0 > 1$, and then the endemic equilibrium point E^* of the dynamical system (1) – (6) is locally asymptotically stable

Proof

The Jacobian matrix of the dynamical system (1)-(6) at the endemic equilibrium point E^* is

$$J(E^*) = \begin{pmatrix} -[dR_0\left(1-\frac{1}{R_0}\right)] - d & 0 & 0 & 0 & -\frac{\beta_1\Lambda}{dNR_0} & 0 \\ dR_0\left(1-\frac{1}{R_0}\right) & -(\omega+d) & 0 & 0 & \frac{\beta_1\Lambda}{\mathrm{d}NR_0} & 0 \\ 0 & p\omega & -(\rho+\alpha+d) & 0 & 0 & 0 \\ 0 & (1-p)\omega & 0 & -(\varepsilon+\epsilon+d) & 0 & 0 \\ 0 & 0 & \alpha & \epsilon & -(\pi+d+d_T) & \theta \\ 0 & 0 & \rho & \varepsilon & \pi & -(\theta+d) \end{pmatrix}$$

The corresponding characteristic equation of the above Jacobian matrix is

$$\begin{vmatrix} -\left[dR_0\left(1-\frac{1}{R_0}\right)\right] - d - \lambda & 0 & 0 & 0 & -\frac{\beta_1\Lambda}{dNR_0} & 0 \\ dR_0\left(1-\frac{1}{R_0}\right) & -(\omega+d)-\lambda & 0 & 0 & \frac{\beta_1\Lambda}{\mathrm{d}NR_0} & 0 \\ 0 & p\omega & -(\rho+\alpha+d)-\lambda & 0 & 0 & 0 \\ 0 & (1-p)\omega & 0 & -(\varepsilon+\epsilon+d)-\lambda & 0 & 0 \\ 0 & 0 & \alpha & \epsilon & -(\pi+d+d_T)-\lambda & \theta \\ 0 & 0 & \rho & \varepsilon & \pi & -(\theta+d)-\lambda \end{vmatrix} = 0$$

After some calculations and using Routh Hurwitz stability criteria we get all the root of the characteristics equation are negative if $R_0 > 1$. Therefore the disease endemic equilibrium point is stable if $R_0 > 1$.

Global stability of the endemic equilibrium point

Theorem

If $S = \mathrm{S}^*, E_T = {E_T}^*, L_f = {L_f}^*, L_s = {L_s}^*, I_T = {I_T}^*$ and $R = R^*$ then the endemic equilibrium point of the dynamical system (1) – (6) is globally asymptotically stable if

$\left(\frac{\boldsymbol{S}-\mathbf{S}^*}{\boldsymbol{S}}\right)\boldsymbol{\Lambda} + \left(\frac{\boldsymbol{E_T}-{\boldsymbol{E_T}}^*}{\boldsymbol{E_T}}\right)\frac{\boldsymbol{\beta_1 I_T}}{\boldsymbol{N}}\boldsymbol{S} + \left(\frac{\boldsymbol{L_f}-{\boldsymbol{L_f}}^*}{\boldsymbol{L_f}}\right)\boldsymbol{p\omega E_T} + \left(\frac{\boldsymbol{L_s}-{\boldsymbol{L_s}}^*}{\boldsymbol{L_s}}\right)(\mathbf{1}-\boldsymbol{p})\boldsymbol{\omega E_T} + \left(\frac{\boldsymbol{I_T}-{\boldsymbol{I_T}}^*}{\boldsymbol{I_T}}\right)(\boldsymbol{\alpha L_f} + \boldsymbol{\epsilon L_s} + \boldsymbol{\theta R}) + \left(\frac{\boldsymbol{R}-\boldsymbol{R}^*}{\boldsymbol{R}}\right)(\boldsymbol{\rho L_f} + \boldsymbol{\varepsilon L_s} + \boldsymbol{\pi I_T}) <$

$$\left[\left(\frac{S-S^*}{S}\right)\frac{\beta_1 I_T}{N}S+\left(\frac{S-S^*}{S}\right)dS+\left(\frac{E_T-E_T{}^*}{E_T}\right)(\omega+d)E_T+\left(\frac{L_f-L_f{}^*}{L_f}\right)(\rho+\alpha+d)L_f+\left(\frac{L_s-L_s{}^*}{L_s}\right)(\varepsilon+\epsilon+d)L_s+ IT-IT*IT\pi+d+dTIT+R-R*R\theta+dR\right.$$

Proof

We define the Liapunov function $L: R_+^6 \to R_+$ by:

$$L(S, E_T, L_f, L_s, I_T, R) = \left\{\begin{array}{c} u_1\left(S - S^* - S^* \ln\left(\frac{S}{S^*}\right)\right) + u_2\left(E_T - E_T{}^* - E_T{}^* \ln\left(\frac{E_T}{E_T{}^*}\right)\right) + \\ u_3\left(L_f - L_f{}^* - L_f{}^* \ln\left(\frac{L_f}{L_f{}^*}\right)\right) + u_4\left(L_s - L_s{}^* - L_s{}^* \ln\left(\frac{L_s}{L_s{}^*}\right)\right) + \\ u_5\left(I_T - I_T{}^* - I_T{}^* \ln\left(\frac{I_T}{I_T{}^*}\right)\right) + u_6\left(R - R^* - R^* \ln\left(\frac{R}{R^*}\right)\right) \end{array}\right\}$$

Thus we get L is continuous function for all $E^* \in \Re_+^6$ and has 1st order partial derivatives and L has minimum at E^*, Finally we calculate the time derivative of $L(S, E_T, L_f, L_s, I_T, R)$ along the solution path yields

$$\Longrightarrow \frac{dL(S,E_T,L_f,L_s,I_T,R)}{dt} = \left\{\begin{array}{c} u_1\left(\frac{dS}{dt} - \frac{S^*}{S}\frac{dS}{dt}\right) + u_2\left(\frac{dE_T}{dt} - \frac{E_T{}^*}{E_T}\frac{dE_T}{dt}\right) + \\ u_3\left(\frac{dL_f}{dt} - \frac{L_f{}^*}{L_f}\frac{dL_f}{dt}\right) + u_4\left(\frac{dL_s}{dt} - \frac{L_s{}^*}{L_s}\frac{dL_s}{dt}\right) + \\ u_5\left(\frac{dI_T}{dt} - \frac{I_T{}^*}{I_T}\frac{dI_T}{dt}\right) + u_6\left(\frac{dR}{dt} - \frac{R^*}{R}\frac{dR}{dt}\right) \end{array}\right\}$$

After some calculation we get $\frac{dL(S,E_T,L_f,L_s,I_T,R)}{dt} = L_1 - L_2$ where

$$L_1 = \left\{\begin{array}{c} \left(\frac{S-S^*}{S}\right)\Lambda + \left(\frac{E_T-E_T{}^*}{E_T}\right)\frac{\beta_1 I_T}{N}S + \left(\frac{L_f-L_f{}^*}{L_f}\right)p\omega E_T + \left(\frac{L_s-L_s{}^*}{L_s}\right)(1-p)\omega E_T + \\ \left(\frac{I_T-I_T{}^*}{I_T}\right)(\alpha L_f + \epsilon L_s + \theta R) + \left(\frac{R-R^*}{R}\right)(\rho L_f + \varepsilon L_s + \pi I_T) \end{array}\right\} > 0 \text{ , and also}$$

$$L_2 = \left\{\begin{array}{c} \left(\frac{S-S^*}{S}\right)\frac{\beta_1 I_T}{N}S + \left(\frac{S-S^*}{S}\right)dS + \left(\frac{E_T-E_T{}^*}{E_T}\right)(\omega+d)E_T + \left(\frac{L_f-L_f{}^*}{L_f}\right)(\rho+\alpha+d)L_f + \\ \left(\frac{L_s-L_s{}^*}{L_s}\right)(\varepsilon+\epsilon+d)L_s + \left(\frac{I_T-I_T{}^*}{I_T}\right)(\pi+d+d_T)I_T + \left(\frac{R-R^*}{R}\right)(\theta+d)R \end{array}\right\} > 0$$

Therefore we conclude that if $L_1 < L_2$ then, $\frac{dL(S,E_T,L_f,L_s,I_T,R)}{dt} < 0$ which implies the endemic equilibrium point for the tuberculosis model is globally asymptotically stable.

Numerical Simulations

In this section we give numerical simulation for dynamical system (1) – (6) for the purpose of verifying some of the analytical results. This is done by using a set of parameter values whose sources are mainly from literature as well as estimation and calculated from assumed date in order to have more realistic simulation results. In this analysis we discuss the effect of each parameters change on the basic reproduction number graphically using win plot software. We assume that initial data of Tuberculosis in Ethiopia in 2010 namely, $N = 107534882$, $S(0) = 101634882$, $E_T(0) = 2500000$, $L_f(0) = 200000$, $L_s(0) = 3000000$, $I_T(0) = 150000 R(0) = 50000$, $d = 0.014286$ and $\Lambda = dN = 44897.96$.

The others parameter are in text on Table-1, which presents the parameter values and their respective sources.

PARAMETER ESTIMATION FOR NUMERICAL SIMULATION AND SENSTIVITY ANALYSIS

To perform numerical simulation and sensitivity analysis we collect the following parameter values obtained from different sources.

Parameter	Formual	Symbol	Value	Source
recruitment rate		Λ	44898 /year	Calculated from Estimated date
effective contact rate		β_1	varied	Estimated
Probability developed to fast latent		p	0.45	Estimated
progression rate from exposed to latent infection	$\frac{1}{\text{Aver.}\,incub.\,period}$	ω	0.166667/yr	Calculated
recovery rate from fast latent by post exposure vaccination		ρ	40/yr	Estimated
progression rate from fast latent to infected	$\frac{1}{\frac{15+365}{2}}$	α	0.0052632	Calculated

progression rate from slow latent to infected	$\frac{1}{\frac{5*365+10*365}{2}}$	ϵ	0.000365297	Calculated
recovery rate from slow latent by post exposure vaccination		ε	25/yr	Estimated
recovery rate from infected class		π	0.25	Estimated
recurrence rate		θ	0.0833333	Estimated
natural death rate		d	0.014286/ yr	Estimated
induced death rate		d_T	0.35 /year	[23]

Table-1: Parameter estimation

Estimation of basic reproduction number R_0

$R_0 = \frac{p\omega\beta_1(\varepsilon+\epsilon+d)[\alpha(\theta+d)+\rho\theta]+(1-p)\omega\beta_1(\rho+\alpha+d)[\epsilon(\theta+d)+\theta\varepsilon]}{(\omega+d)(\rho+\alpha+d)(\varepsilon+\epsilon+d)[(\pi+d+d_T)(\theta+d)-\theta\pi]}$

$R_0 = 1.6684 > 1$

From this value of basic reproduction number we find that the disease spreads in the community as $R_0 = 1.6684 > 1$

Numerical simulation

The numerical analysis is obtained from the graphs of basic reproduction number with respect to the parameters obtained and given in Table-1.

Case-1:

Graphical representation of the basic reproduction number R_0 versus effective contact rate β_1 and keeping other parameters constant

Case-2:

Graphical representation of the basic reproduction number R_0 versus progression rate from exposed to latent infection ω and keeping other parameters constant

For these two cases (1 and 2) the graphical representation of the basic reproduction number in (R_0, β_1) and (R_0, ω)-plans shown below in figure-2 and figure-3 respectively.

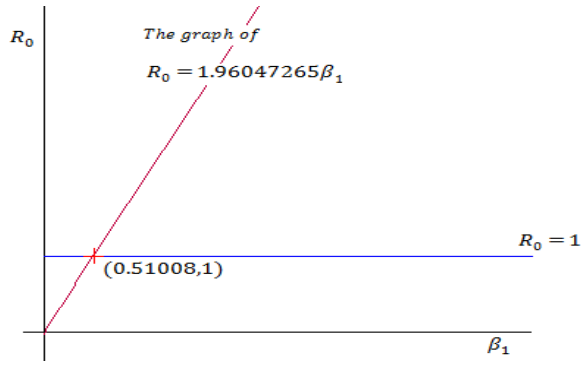

Figure-2

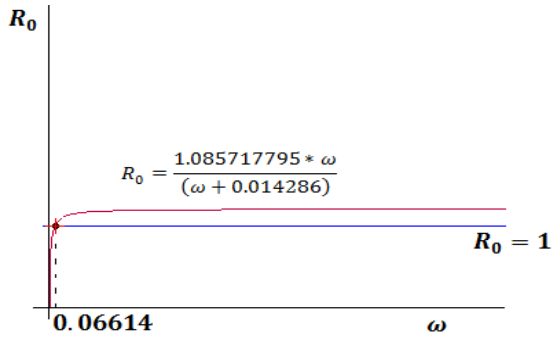

Figure-3

In figure-2: The graph shows that the basic reproduction number $R_0 < 1$ when $\beta_1 < 0.51008$ and $R_0 > 1$ when $\beta_1 > 0.51008$.

In figure-3: The graph shows that the basic reproduction number $R_0 < 1$ when $\omega < 0.1666632$ and $R_0 > 1$ when $\omega > 0.1666632$ with the bifurcation parameter value $\beta_1 = 0.510082$.

Case-3:

Graphical representation of the basic reproduction number R_0 versus recovery rate from fast latent by post exposure vaccination ρ and keeping other parameters constant

Case-4:

Graphical representation of the basic reproduction number R_0 versus progression rate from fast latent to infected α and keeping other parameters constant

For these two cases (3 and 4) the graphical representation of the basic reproduction number in (R_0, ρ) and (R_0, α)-plans shown below in figure-4 and figure-5 respectively.

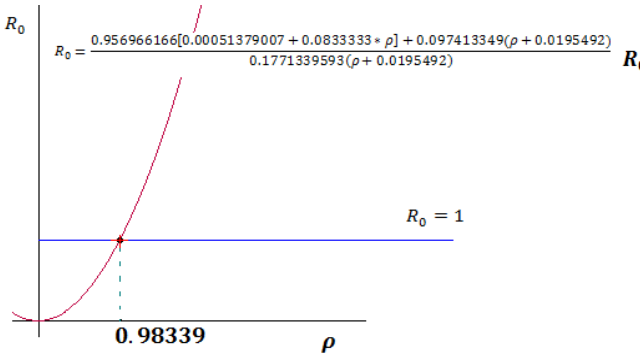

Figure-4

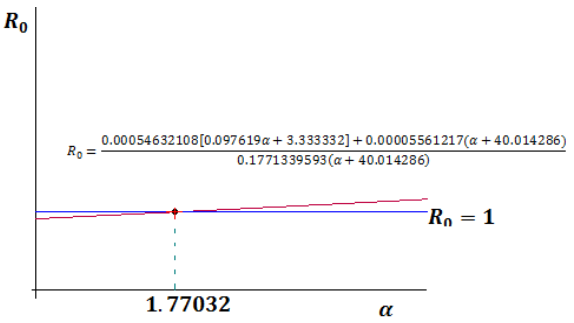

Figure-5

In figure-4: The graph shows that the basic reproduction number $R_0 < 1$ when $\rho < 0.98339$ and $R_0 > 1$ when $\rho > 0.98339$.

In figure-5: The graph shows that the basic reproduction number $R_0 < 1$ when $\alpha < 1.77032$ and $R_0 > 1$ when $\alpha < 1.77032$

Case-5:

Graphical representation of the basic reproduction number R_0 versus progression rate from slow latent to infected ϵ and keeping other parameters constant

Case-6:

Graphical representation of the basic reproduction number R_0 versus recovery rate from slow latent by post exposure vaccination ε and keeping other parameters constant

For these two cases (5 and 6) the graphical representation of the basic reproduction number in (R_0, ϵ) and (R_0, ε)-plans shown below in figure-6 and figure-7 respectively.

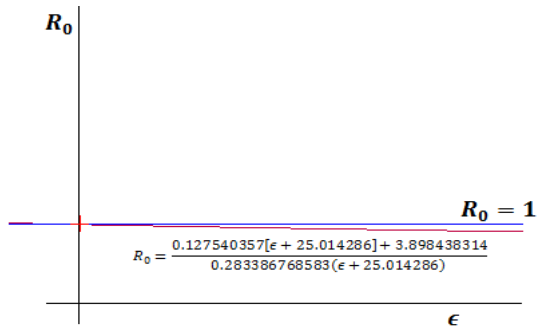

Figure-6

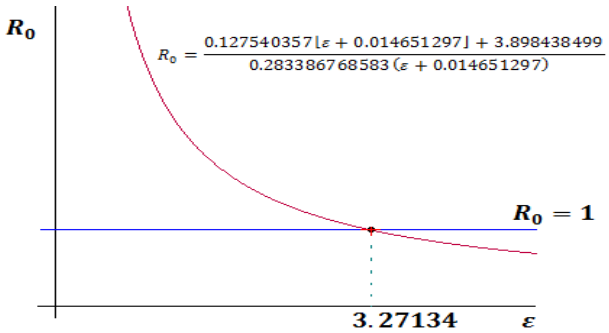

Figure-7

In figure-6: The graph shows that the basic reproduction number $R_0 < 1$ when $\epsilon > 0.00033$ and $R_0 > 1$ when $\epsilon < 0.00033$.

In figure- 7: shows that the basic reproduction number $R_0 < 1$ when $\varepsilon > 3.27134$ and $R_0 > 1$ when $\varepsilon < 3.27134$.

Case-7:

Graphical representation of the basic reproduction number R_0 versus recovery rate from infected class π and keeping other parameters constant

Case-8: Graphical representation of the basic reproduction number R_0 versus recurrence rate θ and keeping other parameters constant

For these two cases (7 and 8) the graphical representation of the basic reproduction number in (R_0, π) and (R_0, θ)-plans shown below in figure-8 and figure-9 respectively.

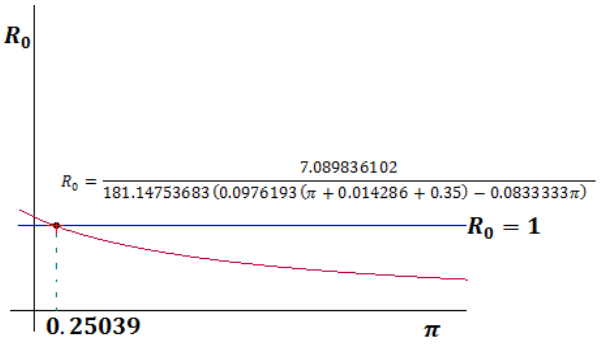

Figure-8

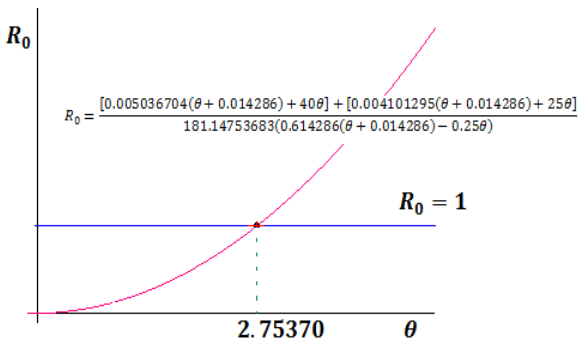

Figure-9

In figure-8: The graph shows that the basic reproduction number $R_0 < 1$ when $\pi > 0.25039$ and $R_0 > 1$when $\pi < 0.25039$

In figure-9: The graph shows that the basic reproduction number $R_0 < 1$ when $\theta < 2.75370$ and $R_0 > 1$ when $\theta > 2.75370$

Sensitivity Analysis

To determine how best we can do in order to reduce human mortality and morbidity due to TB, it is necessary to know the relative importance of different factors responsible for its transmission and prevalence. Sensitivity indices allow us to measure the relative change in a state variable when a parameter changes. The normalized forward sensitivity index of a variable, u , that depends differentially on a parameter, p is calculated by $\psi_p^u = \frac{p}{u} x \frac{\partial u}{\partial p}$. After some simplifications and numerical calculation we get values of sensitivity index for the important parameters mentioned by the table below:

Parameters	Values of sensitivity index
β_1	+1
ω	+0.078949381
ρ	+0.000149635
α	+0.0000101530467
ϵ	+0.000092649909
ε	-0.549619131
π	-0.091265923
θ	+0.9998864
d_T	-0.873095459

Table-2: sensitivity indices

II. Results and Discussions

We discussed on the system of nonlinear ordinary differential equation to study the dynamics of Tuberculosis. Under this we take an appropriate mathematical model on the epidemic of tuberculosis and we found that an important aspect of mathematical epidemiology which is known as basic reproduction number R_0 is determining how to spread and control Tuberculosis. From figure 2, 3, 4, 5 and 9 the effective contact rate β_1, the progression rate from exposed to latent infection ω, the recovery rate from fast latent by post exposure vaccination ρ , and the progression rate from fast latent to infected α and the recurrence rate θ have a positive effect on the basic reproduction number R_0. Figure 2 shows that the rate of conversion from susceptible class to exposed class is increase by due to the contact of infected class with the susceptible class, and the number of infected individuals is increase. So we control the effective contact rate $\beta_1 < 0.51008$ to control $R_0 < 1$. Figure 3 shows that if the progression rate from exposed to latent infection ω increase, then the basic reproduction number R_0 increase. So we control the progression rate from exposed to latent infection $\omega < 0.06614$ to control $R_0 < 1$. Figure 4 shows that the recovery rate from fast latent by post exposure vaccination ρ has a quadratic indirect effect on the basic reproduction number R_0 that means if recovery rate from fast latent by post exposure vaccination is increase the number of recovered individuals having lower immunity are increase. This implies that recurrence rate of infected individuals are increase. That is reproduction number R_0 increases. So we control the recovery rate from fast latent by post exposure vaccination $\rho < 0.98339$ to control $R_0 < 1$. Figure 5 shows that if the progression rate from fast latent to infected α increase, then the basic reproduction number R_0 increases. So we control the progression rate from fast latent to infect $\alpha < 1.77032$ to control $R_0 < 1$. Figure 9 show that if the recurrence rate θ increases then the basic reproduction number R_0 increase. So we control the recurrence rate $\theta < 2.75370$ to control $R_0 < 1$.

From figure 6, 7 and 8 the progression rate from slow latent to infected ϵ , recovery rate from slow latent by post exposure vaccination ε and the recovery rate from infected class π have a negative effect on the basic reproduction number R_0. Figure 6 shows if the progression rate from slow latent to infected ϵ increase implies that number of infected population with non-symptom decreases. Then due to getting active tuberculosis they must get treatment and decrease number of infected populations, and then the basic reproduction number R_0 decreases. So we control the progression rate from slow latent to infect $\epsilon > 0.00033$ to control $R_0 < 1$. Figure 7 show if the recovery rate from slow latent by post exposure vaccination ε increase implies that the number of recovered individuals having high immunity is increase. So we control the recovery rate from slow latent by post exposure vaccination

$\varepsilon > 3.27134$ to control $R_0 < 1$. Figure 8 shows if the recovery rate from infected class π increase implies that number of infected population with active Tuberculosis decreases, then the basic reproduction number R_0 decreases. So we control the recovery rate from infected class $\pi > 0.25039$ to control $R_0 < 1$.

III. Conclusions and Recommendations

The purpose of this study was to develop a mathematical model for Tuberculosis with post exposure vaccination at fast and slow latent stage. Based on the data we have obtained unstable disease free equilibrium point, stable endemic equilibrium point and the basic reproduction number

$R_0 = 1.6684 > 1$ shows that the disease spreads in the community. To control the disease we make the control parameter $\beta_1 < 0.510082$. Also to control the disease giving post exposure vaccination for all slow latent infected individuals and giving post -exposure vaccination for fast latent infected individuals are not important to control the disease. So the coming researcher will consider effect of pre-exposure vaccination for fast latent infected individuals, age structure and sex.

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