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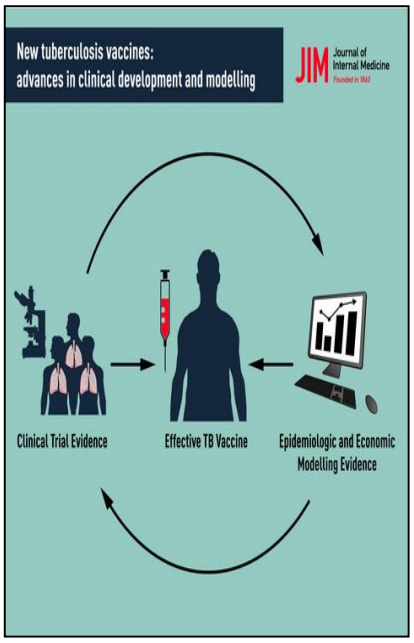
TUBERCULOSIS TRANSMISSION DYNAMICS TREATMENT AND MODELLING EFFECT OF VACCINATION



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ABSTRACT

Tuberculosis (TB) is an airborne and highly contagious disease caused by Mycobacterium tuberculosis. A susceptible person becomes infected with the bacteria when they inhale TB germs, which are released into the air when an infected person coughs, sneezes, spits, or speaks. The fight against tuberculosis includes vaccination with Bacillus calmet-Gurin (BCG), screening for high-risk people, early detection, and treatment of cases. In most TB local countries, BCG vaccination is recommended for tuberculosis prevention and is usually given shortly after birth to prevent tuberculosis in young children.

KEY-WORDS : *Tuberculosis (TB), infected person coughs, sneezes, spits.*

INTRODUCTION

Globally, tuberculosis is a major global health problem and is one of the top multiple causes of death and the leading cause of a single infectious agent. In Ethiopia, TB is still a serious public health challenge and one of the leading causes of morbidity and mortality. According to the same report, TB caused an estimated 25,500 deaths, excluding HIV-related deaths. .

Mathematical models and computer simulations are inexpensive, easy to manage, relatively fast, and fairly productive experimental tools. They have been used extensively to monitor, elucidate, and predict the dynamics of infectious disease transmission. Waller et al began with the first mathematical model of TB. [7], various mathematical models for tuberculosis have been developed, analyzed and used. These models apply to different types of populations such as cities or countries, schools, prisons or refugee camps, see for example. Also, different models will focus on different factors like progress rate, treatment, vaccination, immigration etc....

Mathematical models have been applied for many years to study the transmission dynamics of TB. For example, Zhao it al. [13] The role of age in TB transmission in mainland China was examined and it was found

that the BCG vaccine is only useful for young people. He also suggested that the DOTS program should be more focused on the senior-elderly group and more focused on people with latent TB in middle age. Choi et.al.introduced three control mechanisms: distance, case detection and case holding in SEIL model in South Korea. He showed that distance control is the most effective preventive measure. Mauleu et al. on the other hand. Developed a model for TB's transmission dynamics and applied it to Cameroon's data. They recognized that the combined efforts of education and chemoprophylaxis could lead to an 80% reduction in the number of infected people in 10 years. Kim et al. developed mathematical models for tuberculosis and adapted to Philippine data. Their results showed that applying a combination of distance and case detection strategies has significant potential to reduce the prevalence of TB in the Philippines. That is why the transmission dynamics of TB through mathematical models is important to propose the best mechanism to control the spread of TB. The purpose of this study is to develop a suitable TB dynamics model and to calibrate it for Ethiopia.

MATERIAL AND METHODS:

Formulation of Model:

We assume that the population has an enrollment rate Λ and part of it$\varepsilon\Lambda$, will be vaccinated at birth where$0 \leq \varepsilon \leq 1$. The natural mortality rate (any death that is not due to TB) is assumed to be the same for each class and the mortality rate due to TB is indicated to be the same in I-class δ. The efficacy of the BCG vaccine is not complete. Therefore, it is assumed that some of the vaccinated individuals will be susceptible to bacteria at a rate of θ.

Infectious individuals can be infected with TB through a transmission coefficient β. The treatment rate for the class is indicated by . It is assumed that the untreated part of E-class will develop active TB k. If treated for I-class at a rate of *r*, some of them will complete their treatment properly$(1-p)(0 \leq p \leq 1)$. Healed individuals are moved to the *L*-class because treatment cannot destroy the tuberculosis bacteria from the patient's body. Therefore, infected individuals after recovery and low-risk are classified into a single class of low-risk dormant individuals. Tuberculosis is assumed to have no permanent immunity so some cured individuals may lose immunity and become at high-risk-latent infection, with a recurrence rate . We further assume that all the parameters used in this model are negative.Based on our definitions, assumptions and correlations in variables, the ODE system describing the dynamics of TB has been developed as follows.

$$\begin{cases} \frac{dS}{dt} = (1-\varepsilon)\Lambda + \theta V - \beta SI - \mu S \\ \frac{dV}{dt} \varepsilon\Lambda - (\theta+\mu)V \\ \frac{dE}{dt} = \beta SI + prI + \sigma L - (k+\alpha+\mu)E \\ \frac{dI}{dt} = kE - (\mu + r + \delta)I \\ \frac{dL}{dt} = (1-p)rI + \alpha E - (\mu+\sigma)L \\ N(t) = S(t) + V(t) + E(t) + I(t) + L(t) \end{cases} \qquad \text{Equation – 1}$$

Basic Properties:

Theorem 1: Let the initial data S_0, V_0, E_0, I_0 and L_0 be negative. Then set the solution> 0.

Proof:

We use the second module from equation – 1

$$\frac{dV(t)}{dt}\varepsilon\Lambda - (\theta + \mu)V$$

Equation -2

For the simplicity it will write $\theta + \mu = \varphi$and $\varepsilon\Lambda = \lambda$, then

$$\frac{dV(t)}{dt} + \varphi\mathrm{V}(t) = \lambda$$

Equation – 3

Multiplying both sides of equation 3 by exponential (φt) it gives,

$$\frac{dV(t)}{dt}\exp(\varphi t) + \varphi\mathrm{V}(t)\ exp\ (\varphi t) = \lambda exp(\varphi t)$$

Equation – 4

According to the production regulations of the derivatives we have

$$\frac{dV(t)}{dt}\exp(\varphi t) + \varphi\mathrm{V}(t)\ exp\ (\varphi t) = \frac{d}{dt}[V(t)\exp(\varphi t)]$$

Equation – 5

Due to from equation – 4 we can have following…

$$\frac{d}{dt}[V(t)\exp(\varphi t)] = \lambda exp(\varphi t)$$

Equation – 6

Let's combine both sides of Equation 6

$$V(t) = V(e)\exp(-\varphi t) + \frac{\lambda}{\varphi}(1 - \exp(-\varphi t)) \geq 0$$

Equation – 7

Similarly, let's take the first equation of (1)

$$\frac{ds(t)}{dt} = (1 - \varepsilon)\Lambda + \theta\mathrm{V} - \beta SI - \mu S(t)$$

Equation – 8

By letting $(1 - \varepsilon)\Lambda = \varphi\ and\ (\beta I(t) - \mu) = H(t), we\ have$

$$\frac{ds(t)}{dt} + H(t)S(t) = \emptyset + \theta V(t)$$

Equation – 9

Multiply both side of equation – 9 by $\exp\left\{\int_0^t H(\tau)d\tau\right\}$gives

$$\frac{ds(t)}{dt}exp\left\{\int_0^t H(\tau)d\tau\right\}+H(t)S(t)exp\left\{\int_0^t H(\tau)d\tau\right\}=\emptyset exp\left\{\int_0^t H(\tau)d\tau\right\}+\theta V(t)\exp\left\{\int_0^t H(\tau)d\tau\right\}$$

Equation – 10

By the production rule of derivatives, we have

$$\frac{ds(t)}{dt}exp\left\{\int_0^t H(\tau)d\tau\right\}+H(t)S(t)exp\left\{\int_0^t H(\tau)d\tau\right\}=\frac{d}{dt}\left[S(t)exp\int_0^t H(\tau)d\tau\right]$$

Equation – 11

Hence due to that,

$$\frac{d}{dt}\left[S(t)exp\int_0^t H(\tau)d\tau\right]=\emptyset\, exp\left\{\int_0^t H(\tau)d\tau\right\}+\theta V(t)exp\left\{\int_0^t H(\tau)d\tau\right\}$$

Equation – 12

Integrating both side of equation 12 gives…

$$S(t)exp\left\{\int_0^t H(\tau)d\tau\right\}-S_0=\emptyset\int_0^t exp\left\{\int_0^t H(u)du\right\}+\int_0^t \theta V(u)exp\left\{\int_0^t H(u)du\right\}$$

Equation – 13

$$S(t)=S_0exp\left\{-\int_0^t H(\tau)d\tau\right\}+\left[\emptyset\int_0^t exp\left\{\int_0^t H(u)du\right\}\right]\left[exp\left\{-\int_0^t H(\tau)d\tau\right\}\right]+\left[\theta V(u)exp\int_0^t H(u)du\right]$$
$$-\left[\theta V(u)exp\int_0^t H(u)du\right]\geq 0$$

Equation – 14

Similarly, we can show that *E(t),I(t)*and *L(t)* are negative. Notice, in particular, that it follows from

Equation-13

$$\lim_{t\to\infty} V(t)=\frac{\varepsilon\Lambda}{\theta+\mu}$$

Equation – 15

Invariant Regions:

Theorem 2: With non-negative initial conditions, the viable region of the model is defined

$$\Omega=\left\{(S(t),V(t),E(t),I(t),L(t))\,\epsilon\mathbb{R}_+^5\,\middle|\,S(t)+V(t)+E(t),I(t),L(t)\leq\frac{\Lambda}{\mu}\right\}$$

Equation – 16

Proof:

Change of total population size is at…

$$\frac{dN(t)}{dt} = \frac{ds(t)}{dt} + \frac{dV(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI(t)}{dt} + \frac{dL(t)}{dt} = \Lambda\mu N(t) - \delta I(t) \leq \Lambda - \mu N(t)$$

Equation – 17

The inequality of equation 17

$$N(t) \leq \frac{\Lambda}{\mu} - N_0 \exp(-\mu t)$$

Equation – 18

Due to that for every t>0, as $t \to \infty, N(t) \leq \frac{\Lambda}{\mu}$, due to that the invariant region for this model is

$$\Omega = \left\{(S(t), V(t), E(t), I(t), L(t)) \epsilon \mathbb{R}_+^5 \middle| S(t) + V(t) + E(t), I(t), L(t) \leq \frac{\Lambda}{\mu}\right\}$$

Equation – 19

Analysis of the Model:

Disease-Free Equilibrium Point and the Elementary Imitation Number, the disease-free equilibrium point of the model (1) is given by:

$$P_0^* = (S_0^*, V_0^*, 0,0,0)$$

Equation -20

Where,

$S_0^* = \Lambda/\mu\left(\theta + \mu(1-\varepsilon)\right)/(\theta + \mu)$

$V_0^* = \varepsilon\Lambda/\mu\,(\theta + \mu)$

The basic reproduction number (R_0) is the expected average number of new TB infections caused by a single infected person when in contact with a fully susceptible population. We obtained R_0 using the next generation matrix method given in Equation 17, to calculate the two matrices *M* and *F*, where *M* is the rate of transfer of individuals in and out of the transition classes and *F* is the new rate of transition in the box. So, by the equations we get,

$$F = \begin{pmatrix} 0 & \beta\Lambda\left(\frac{1}{\mu} - \frac{\varepsilon}{\theta+\mu}\right) & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

Equation – 21

$$M = \begin{pmatrix} k+\alpha+\mu & -pr & -\sigma \\ -k & r+\delta+\mu & 0 \\ -\alpha & (-1+p)r & \mu+\sigma \end{pmatrix}$$

Equation – 22

Then R_0 is the prime eigenvalue of matrix F^{-1}.

Due to which we have,

$$\Re_0 = (k\beta\Lambda[\theta + \mu(1-\varepsilon)]\mu + \sigma)/\mu(\theta+\mu)\,[\mu(r+\delta+\mu)(\alpha+\mu+\sigma) + k\{r\mu(1-p) + (\delta+\mu)(\mu+\sigma)\}]$$

The following number,$\mathcal{R}_g$serves as an indicator for the global stability of the disease-free equilibrium point:

$$\mathcal{R}_g = \frac{k\beta\Lambda[\theta + \mu(1-\varepsilon) + \eta]}{\mu(\theta+\mu)[\mu_1\mu_2 - kpr]}$$

Equation – 23

Where,

$$\mu_1 = \alpha + \mu + k$$

$\mu_2 = r + \delta + \mu$and

$$\eta = (\mu\sigma/k\beta\Lambda)[\alpha\mu_1 + (1-p)rk]$$

Theorem 3:

For model (1), if the disease-free equilibrium point is P_0^* Rg <1 then globally asymptomatic is stable$\mathcal{R}_g$.

We follow the same procedure as the stability analysis of Equations 18 and 19.

For $\mathcal{R}_g < 1$ we have,

$$\frac{k\beta\Lambda[\theta + \mu(1-\varepsilon) + \eta]}{\mu(\theta+\mu)} - [\mu_1\mu_2 - kpr] < 0$$

Equation – 24

We can write this in following….

$$\frac{k\beta\Lambda[\theta + \mu(1-\varepsilon)]}{\mu(\theta+\mu)} + \frac{k\beta\Lambda\eta}{\mu(\theta+\mu)} - [\mu_1\mu_2 - kpr] < 0$$

Equation – 25

By the Archimedes property of $\mathcal{R}_g$, exists $\gamma_0 > 0$, for which

$$\frac{k\beta\Lambda[\theta + \mu(1-\varepsilon)]}{\mu(\theta+\mu)} + \gamma_0 k\beta + \frac{k\beta\Lambda\eta}{\mu(\theta+\mu)} - [\mu_1\mu_2 - kpr] < 0$$

Equation – 26

Along with this we can find a number γ_1 with $0 < 1 < \mu$ and such that

$$\frac{k\beta\Lambda[\theta + \mu(1-\varepsilon)]}{\mu(\theta+\mu)} + \gamma_0 k\beta + \frac{k\beta\Lambda\eta}{\mu(\theta+\mu)}\frac{\sigma+\gamma_1}{\gamma_1}$$

Equation – 27

We need upper bound for *S(t)*, from the comment of Equation 15 it appears that there exists as t_0. Such that $|V(t) - \varepsilon\Lambda/(\theta+\mu)| < \gamma_0$whenever $t < t_0$.Without compromising normalcy, we can assume so$|V(t) - \varepsilon\Lambda/(\theta+\mu)| < \gamma_0$whenever $t > 0$

The inequality in the latter suggests this$\varepsilon\Lambda/(\theta+\mu) - \gamma_0 < V(t)$ and consequently, that $-V(t) - \varepsilon\Lambda/(\theta+\mu) + \gamma_0$ along with we have,

$$N(t) \leq \Lambda/\mu$$

Due to for every t > 0,

$$S(t) \leq N(t) - V(t) > \frac{\Lambda}{\mu} - \frac{\varepsilon\Lambda}{\theta+\mu} + \gamma_0 = \frac{\Lambda}{\mu}\frac{\theta+\mu(1-\varepsilon)}{\theta+\mu} + \gamma_0$$

Equation – 28

Now taking $\gamma_2 = \gamma_1/2$we present two constants C_0 and C_1 as follows:

$$C_0 = \frac{\mu_2}{k} - \frac{\alpha(\sigma+\gamma_1)}{k(\mu+\sigma)}$$

Equation – 29

$$C_1 = \frac{\sigma+\gamma_1}{\mu+\sigma}$$

Equation – 30

In particular than, $C_0 > 0$

Now we define a function:

$$Q(t) = E(t) + C_0 I(t) + C_1 L(t)$$

Equation – 31

We now prove that --- is negative-certain, remember that we can write

$$Q(t) = C_2 E + C_3 I + C_4 L$$

Equation – 32

Where,

$$C_2 = C_0 k - \mu_2 + C_1\alpha,$$
$$C_3 = \beta S + pr - C_0\mu_1 + (1-p)rC_1, and$$
$$C_4 = \sigma - C_1(\mu+\sigma)$$

Then

$$C_4 = -\gamma_2 < 0$$
$$C_2 = -\frac{\alpha(\sigma+\gamma_1)}{(\mu+\sigma)} + \frac{\alpha(\sigma+\gamma_2)}{(\mu+\sigma)} = \frac{\alpha(\gamma_1+\gamma_2)}{(\mu+\sigma)}$$

Equation – 33

Since $\gamma_2 < \gamma_1$ it follows that $C_2 < 0$, then we can write kC_3 as

$$kC_3 = k(\beta S + pr) - \mu_1\mu_2 + C_5$$

Equation – 34

Where,

$$C_5 = \frac{\mu_1\alpha(\sigma+\gamma_1) + rk(1-p)(\sigma+\gamma_2)}{\mu+\sigma} \leq \frac{\sigma+\gamma_1}{\mu+\sigma}[\mu_1\alpha + rk(1-p)] = \frac{(\sigma+\gamma_1)k\beta\Lambda}{\sigma\mu(\theta+\mu)}\eta$$

Equation – 35

Also note the upper constraint *S(t)* we get the following inequality,

$$kC_3 \leq k\left\{\frac{\Lambda\beta}{\mu(\theta+\mu)}[\theta+\mu(1-\varepsilon)]+\gamma_0\beta+pr\right\}-\mu_1\mu_2+\frac{\mathrm{k}\Lambda\beta}{\mu(\theta+\mu)}\frac{\sigma+\gamma_1}{\sigma}\eta$$

Equation – 36

Due to the inequality in Therefore Equation 16, it is that 3 <0,proves that kC_3 the negative is certain. Therefore*Q(t)* this is the Lipunov function Ω therefore, according to Lasalle's Invarians principle in Equation 20, in each solution of model (1), with any initial conditions in the approach P_0^* so $t \to \infty$, Whenever $\mathcal{R}_g < 1$.

The existence of a local equilibrium point,in this section, we show the existence of the local equilibrium point of model (1). The local equilibrium point is the steady state where the disease survives in the population when at least one of the infected classes of the model is not zero.

Theorem 4: if $\mathcal{R}_g > 1$ then there is a unique positive spatial balance in model (1)

$$P^* = (S^*, V^*, E^*, I^*, L^*)$$

Equation – 37

$$S^* = \frac{\Lambda[\theta+\mu(1-\varepsilon)]}{\mathcal{R}_0(\theta+\mu)}$$

Equation – 38

$$V^* = \frac{\varepsilon\Lambda}{\theta+\mu}$$

Equation – 39

$$E^* = \frac{(r+\delta+\mu)\mu}{k\beta}(\mathcal{R}_0-1)$$

Equation – 40

$$I^* = \frac{\mu}{\beta}(\mathcal{R}_0-1)$$

Equation – 41

$$L^* = \frac{\mu\big(kr(1-p)+\alpha(r+\delta+\mu)\big)(\mathcal{R}_0-1)}{k\beta(\mu+\sigma)}$$

Equation – 42

CONCLUSION:

The reproduction number is calculated and the equilibrium points are described. We showed that the disease-free equilibrium point P_0^* is globally asymptotically stable when$\mathcal{R}_0 < 1$, so that the disease ends. Finally, we showed that an increase in the scope of treatment and vaccination leads to a decrease in the number of infected TB patients. The parameter values of the model are obtained from the existing literature and the

annual reports in Ethiopia fit into the incidence of TB. We estimate that the basic reproduction number for TB transmission in Ethiopia is R0 = 2.13. This means that TB is still local in the country and more emphasis should be placed on preventing the spread of TB.

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