Modified SIR Model for Tuberculosis with Latent disease

Gurpreet Singh Tuteja

Zakir Husain Delhi College,

J. L. Nehru Marg, New Delhi -110002, India.

Abstract

In this paper, we have modified the SIR model based on compartment theory [5] to study the mathematical and stability analysis of the transmission dynamics of Tuberculosis by including latent infection. This modified model consists of four compartments SLIR, defined as Susceptible, Latent (infection), Infection and Recover. The susceptible become infected if they are infected by airborne infection mycobacterium and then they move from susceptible compartment to the latent (infected) compartment *(L)* which carries the infection but not infectious. If not treated, becomes infected and infectious, moves to the compartment infection *(I)*. The treatment is a long procedure, many a time the infected feels better and doesn't complete the treatment. Thus, patient instead of recovering completely moves back to the latent (infection) compartment, wherein the bacteria remain inactive for a while. As soon as bacteria become active, latently infected returns to the infection compartment. The governing differential equations are defined. The reproduction number R_0 of the model is calculated using the Jacobian matrix method [6]. A brief of stability and numerical analysis is also done.

1. Introduction

Tuberculosis is an airborne infection caused by the Mycobacterium Tuberculosis (MTB) bacilli. The disease tuberculosis is an ancient scourge. It has plagued humankind throughout known history and human prehistory [1]. It is therefore important to model infectious diseases so that they can be managed and the epidemic can be reduced. The various mathematical models are used to study the process by which the progress of epidemic can be understood and controlled. It is anticipated that the ability to make disease predictions would enable scientists to understand its growth in the population so that inoculation or isolation plans can be planned effectively.

Roughly 4 million people each year who develop TB disease who are undiagnosed, unreported, or inappropriately treated [11]. The widespread availability of vaccines, an arsenal of anti-microbial drugs and, more recently, a highly viable attempt by the World Health Organization to promote a single global control, after several decades of research is being managed successfully.

A basic definition of three interacting compartments: Susceptibility (S), Infected (I), and Recovered (R), is given by the SIR model [3][4][5] in epidemiology. The SIR model, despite its simplicity, exhibits the basic structure to understand the dynamics of contagious diseases. In recent years, several variants of the SIR model have been studied to model effectively more complex diseases and mechanisms of infection. The SIR model has been used to study the progression of Tuberculosis [9][10].

In this paper, we modify the SIR model by introducing a compartment termed as latent (infected) to study the dynamics of tuberculosis and the incidence function assumed to be bilinear. The paper is organised as follows: In section 2, we state the mathematical equations of the model. In section 3, the basic reproduction number computed and the stability of equilibrium points using Lyapunov function. Section 4 discusses the importance of the parameters related to latent (infected) and graphically using numerical solution followed by the conclusion as section 5.

2. Mathematical Model

The TB bacteria target any part of the body including skin, lung, kidney, spine and brain. Not everybody who is affected by TB (Tuberculosis) bacteria gets ill. As a result, there are two conditions linked to TB: latent infection with TB (LTBI) and TB disease. TB disease can be fatal if not adequately treated [11].

Here, the modified SIR model of TB transmission is analysed by dividing the human population into four subpopulations, namely, Suspected S, latent L, Infected I, and Recovered R. The movement of the population is defined in ***Fig. 1***. The rate of birth, death is Λ and μ, respectively. The rate of susceptible to infected (latent) and recovered is β and δ, the rate of infected to recover is γ. The treatment for tuberculosis symptoms can last anywhere from six months to a year, and sometimes more for drug-resistant tuberculosis. The recovered population moves back to susceptible as a different strain of tuberculosis causing bacteria can infect. TB recurrence can be caused either by reactivation of the same strain (i.e. by relapse primarily due to unsuccessful or incomplete treatment) or by new strain reinfection, which means that a TB patient after recovering doesn't acquire any immunity [8]. So, the recovered population moves to susceptible again with a rate σ.

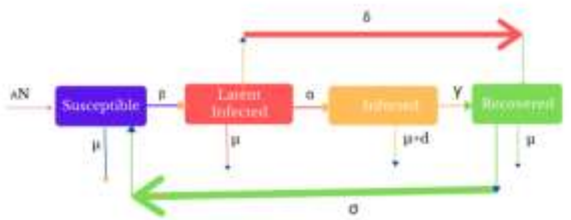


Fig. 1: Modelling TB with Latent Infection

The governing differential equations of the above model (***Fig.1***) are:

$$\frac{dS}{dt} = \Lambda N - \frac{\beta\, S(t)I(t)}{N} - \mu\, S(t) + \sigma R(t) \qquad (1)$$

$$\frac{dL}{dt} = \frac{\beta\, S(t)I(t)}{N} - (\mu + \delta + \alpha)L(t) \qquad (2)$$

$$\frac{dI}{dt} = \alpha L(t) - (\mu + d + \gamma)I(t) \qquad (3)$$

$$\frac{dR}{dt} = \gamma I(t) + \delta L(t) - (\sigma + \mu)\, R(t) \qquad (4)$$

Where $N(t) = S(t) + L(t) + I(t) + R(t),$ (5)

$S(0)=S_0 > 0$, $L(0)=L_0 \geq 0$, $I(0)=I_0 \geq 0$ and $R(0)=R_0 \geq 0$.

The equations (1) - (5) are re-written using dimensionless variables as:

$S' = S/N$, $L'=L/N$, $I'=I/N$, $R'=R/N$, and further omitting dashes, we obtain

$$\frac{dS}{dt} = \Lambda - \beta\, S(t)I(t) - \mu\, S(t) + \sigma R(t) \qquad (6)$$

$$\frac{dL}{dt} = \beta\, S(t)I(t) - (\mu + \delta + \alpha)L(t) \qquad (7)$$

$$\frac{dI}{dt} = \alpha L(t) - (\mu + d + \gamma)I(t) \qquad (8)$$

$$\frac{dR}{dt} = \gamma I(t) + \delta L(t) - (\sigma + \mu)\, R(t) \qquad (9)$$

Where $1 = S(t) + L(t) + I(t) + R(t),$ (10)

$S(0)=S_0 > 0$, $L(0)=L_0 \geq 0$, $I(0)=I_0 \geq 0$ and $R(0)=R_0 \geq 0$.

3. Conditions of Equilibrium

Positivity of the Solution: We show that the model equations (6 - 9) are biologically and epidemiologically meaningful and well-posed. It is appropriate to show that the solutions of all the stated variables are non-negative. The requirement is stated as theorems and is followed by its proof:

Theorem 1: If *S(0) > 0, L(0) > 0, I(0) > 0 and R(0) > 0* then the solution region *S(t), L(t), I(t) , R(t)* of the system of equations (6 - 9) is always non-negative.

Proof: Consider the system of the equations (6 - 9), each differential equation is discussed separately and shown that its solution is positive.

Theorem 2: *Positivity of infected human population*: Considering (8) and that can be rewritten:

$$\frac{dI}{dt} = \alpha L(t) - (\mu + d + \gamma)I(t) \geq -(\mu + d + \gamma)I(t) \,.$$

On, integrating the solution is $I = I_0 e^{-\int_0^t (\mu+d+\gamma)dt}$. It is clear from the solution that I(t) is positive since $I_0 > 0$ and the exponential function is always positive.

Theorem 3: Positivity of latent infected population: Considering the differential equation (8) of the system

$\frac{dL}{dt} = \beta\, S(t)I(t) - (\mu + \delta + \alpha)I(t) \geq -(\mu + \delta + \alpha)I(t).$

Using the technique of separation of variables and on integrating:

$L = L_0 e^{-\int_0^t (\mu+\delta+\alpha)dt}$.

For any value of the exponent, the exponential term is always a non-negative quantity. Also it is assumed that *L(0) > 0*. Thus, it is clear from the solution that *L(t)* is positive.

Theorem 4: Positivity of recovered: Considering the differential equation (9) of the system

$$\frac{dR}{dt} = \gamma I(t) + \delta L(t) - (\sigma + \mu)R(t) \geq \; -(\sigma + \mu)R(t)$$

The *L(t)* and *I(t)* are positive in time t. On, integrating the solution is $R = R_0 e^{-\int_0^t (\sigma+\mu)dt}$. It is clear from the solution that *I(t)* is positive since $I_0 > 0$ and the exponential function is always positive.

Theorem 5: Positivity of susceptible population: Finally, we consider the differential equation (6):

$$\frac{dS}{dt} = \Lambda - \; \beta\, S(t)I(t) - \mu\, S(t) + \sigma R(t) \; \geq \; - \; \beta\, S(t)I(t) - \mu\, S(t)$$

Λ is the rate of birth and *R(t)*, being positive, we can write as:

$$\frac{dS}{S(t)} = \; -(\; \beta I(t) + \mu) \; dt$$

On, integrating the solution is $S = S_0 e^{-\int_0^t (\beta I(t)+\mu)dt}$. It is clear from the solution that *S(t)* is positive since $S_0 > 0$ and the exponential function is also positive.

The model equations (6-10) are biologically and epidemiologically meaningful and well-posed as the solutions of all the state variables are bounded.

From Equation (6) to (9), as

$$\frac{dS}{dt} + \frac{dL}{dt} + \frac{dE}{dt} + \frac{dR}{dt} = 0$$

$$\Lambda - \mu S(t) = 0$$

Therefore, the feasible region for the system is given by (S*, L*, I*, R*)

$S^* = \frac{\Lambda}{\mu}, L^* = 0, I^* = 0, R^* = 0,$

$$\omega = [(S^*, L^*, I^*, R^*) \in R^{4+} : S^* + L^* + I^* + R^* \leq \frac{\Lambda}{\mu}$$

Hence, it sufficient to consider solutions in the region ω. The solutions of the initial value problem starting in ω and defined by (7) - (10) exist and are unique on a maximal interval. Since the solution remains bounded in the positively invariant region ω, the maximal interval defined is [0, 1). So, the initial value problem is both well-posed and is positive. The above system always has a disease-free equilibrium:

$$\left(\frac{\Lambda}{\mu}, 0, 0, 0,\right)$$

Using the Jacobian Matrix method and differential equations (6)-(9), the Characteristic polynomial is obtained:

$$\frac{(\lambda + \mu)(\lambda + \mu + \sigma)(-\alpha\beta\Lambda + \alpha\mu(d + \lambda + \mu + \Upsilon) + \mu(\delta + \lambda + \mu)(d + \lambda + \mu + \Upsilon))}{\mu}$$

The Eigenvectors are:

$$\lambda_1 = -\mu, \lambda_2 = -\mu - \sigma, \lambda_3 = \frac{-A - \sqrt{\mu}\sqrt{B}}{2\mu}, \lambda_4 = \frac{-A + \sqrt{\mu}\sqrt{B}}{2\mu}$$

where $A = d\mu + \alpha\mu + \delta\mu + 2\mu^2 + \mu\Upsilon$

$B = 4\alpha\beta\Lambda + d^2\mu - 2d\alpha\mu + \alpha^2\mu - 2d\delta\mu + 2\alpha\delta\mu + \delta^2\mu + 2d\mu\Upsilon - 2\alpha\mu\Upsilon - 2\delta\mu\Upsilon + \mu\Upsilon^2$

Also, B can be re-written as:

$$4\alpha\beta\Lambda + \mu(\alpha - d + \delta - \Upsilon)^2 \geq 0$$

Therefore roots are real. Also, λ_1, λ_2, λ_3, are negative and for $\lambda_4 < 0$

$$-A > \sqrt{\mu}\sqrt{B}$$

On substituting values of A and B, simplifying we obtain

$$\frac{\alpha\beta\Lambda}{\mu(\alpha + \delta + \mu)(d + \mu + \Upsilon)} < 1$$

So, we define, basic reproductive number R_0 as,

$$R_0 = \frac{\alpha\beta\Lambda}{\mu(\alpha + \delta + \mu)(d + \mu + \Upsilon)}$$

On solving equation (9) to (11), we obtain

$$S^* = \frac{\Lambda}{R_0\mu},$$

$$L^* = \frac{(-1 + R_0)\Lambda(\mu + \sigma)(d + \mu + \Upsilon)}{PR_0},$$

$$I^* = \frac{(-1 + R_0)\alpha\Lambda(\mu + \sigma)}{PR_0},$$

$$R^* = \frac{(-1 + R_0)\Lambda(d\delta + \alpha\Upsilon + \delta(\mu + \Upsilon))}{PR_0}$$

Where,

$$P = d\alpha(\mu + \sigma) + d\mu(\delta + \mu + \sigma) + \mu(\delta + \mu + \sigma)(\mu + \Upsilon) + \alpha\mu(\mu + \sigma + \Upsilon)$$

Thus, DFE point (Λ/μ, 0, 0, 0) of (6) - (9) is globally asymptotically stable in Ω if $R_0 \leq 1$ and is unstable if $R_0 > 1$.

Now, we find the stability of the endemic equilibrium ($\sigma = 0$) [7]. We consider equation (6), (7) and (8) only.

Consider a Lyapunov function:

$$V = W_1\left(S - S^*\log\frac{S}{S^*}\right) + W_2\left(L - L^*\log\frac{L}{L^*}\right) + W_3\left(I - I^*\log\frac{I}{I^*}\right)$$

Substituting the value of $\dot{S}, \dot{L}$ and $\dot{I}$ from equation (6) and (7) and (8)

$$\dot{V} = W_1(S - S^*)\left(\frac{\Lambda}{S} - \beta I - \mu\right) + W_2(L - L^*)\left(\beta\frac{SI}{L} - (\mu + \delta + \alpha)\right) + W_3(I - I^*)\left(\alpha\frac{I}{L} - (\mu + d + \gamma)\right)$$

Let the equilibrium points be: $\mu = \frac{\Lambda}{S^*} - \beta I^*$, $\mu + \delta + \alpha = \frac{S^*I^*}{L^*}$ and $\mu + d + \gamma = \alpha\frac{I^*}{L^*}$

$$\dot{V} = -W_1(S - S^*)\Lambda\frac{(S - S^*)}{SS^*} + \beta(I - I^*)) + W_2\beta(L - L^*)\left(\frac{SI}{L} - \frac{S^*I^*}{L^*}\right) + W_3(I - I^*)\alpha\left(\frac{I}{L} - \frac{I^*}{L^*}\right)$$

$$\leq -\Lambda W_1\left(\frac{(S - S^*)^2}{SS^*} + \beta(I - I^*)(S - S^*)\right) - \frac{W_2\beta S^*I^*(L - L^*)^2}{LL^*} - \alpha W_3 I^*(I - I^*)(L - L^*)$$

$\dot{V} \leq 0$ for $S < S^*$, $I < I^*$ *and* $L < L^*$, $W_1 = W_2 = W_3 = 1$ and also for $S = S^*$, $I = I^*$, $L = L^*$, $V = 0$.

Therefore, by La Salle's Invariance principle [2], the endemic system is globally asymptotically stable.

4. Numerical Discussion

We use NDSolve function of Wolfram Mathematica to solve dimensionless differential equations (6) to (10) numerically. The numerical solutions of *S, L, I* and *R*, are plotted for different values of parameters. The solutions of *S(t), L (t), I(t)* and *R(t)* for the parameters: $t=100$, $\Lambda=\mu=.01$, $R_0=0.5$, $\gamma=.13$, $\alpha=0.3$, $\sigma=.011$.

Case I: If the TB is diagnosed well within time and treated properly the individual without becoming infectious will recover. The different values for δ = *0.01, 0.05, 0.1*. As the rate of movement from latent infected compartment to the recovered compartment is increased consequently the infected reduces. The peak of the *R(t)* and latent infected *L(t)* increases while the peak of the infection and susceptible reduces (***Fig. 2-4***).

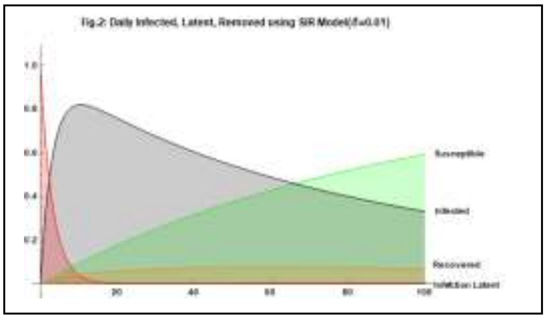


Fig.2: Daily Infected, Latent, Removed using SIR Model(β=0.01)

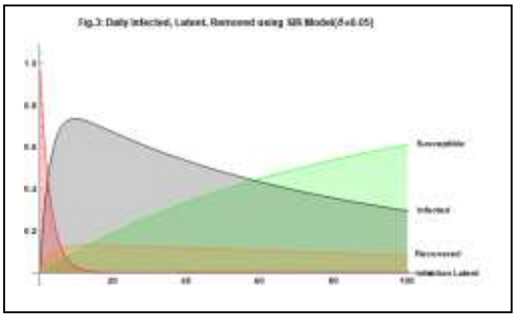


Fig.3: Daily Infected, Latent, Removed using SIR Model(β=0.05)

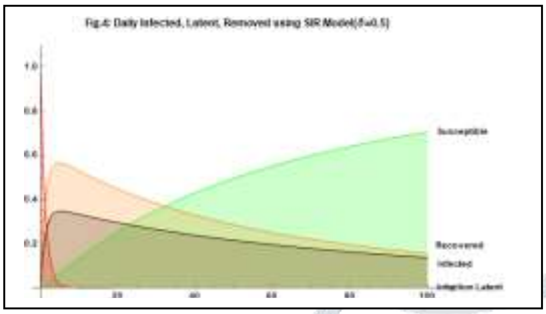


Fig.4: Daily Infected, Latent, Removed using SIR Model(β=0.5)

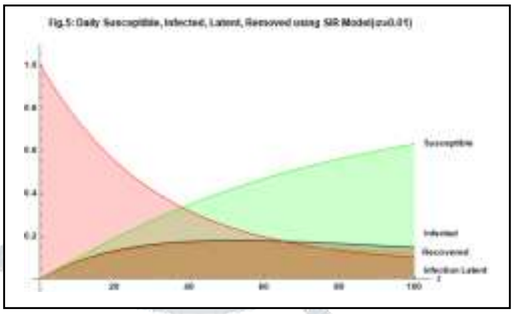


Fig.5: Daily Susceptible, Infected, Latent, Removed using SIR Model(α=0.01)

Case II: Keeping other parameter constants, we vary α, the rate of latent infected *L(t)* to infected *I(t)* depends on the medical facilities available including TB diagnostic tests and follow-up treatments. The patient who completes the treatment successfully will be moved to the compartment recovered else can carry TB latently. As *α* is increased and takes value 0.05, 0.05 and 0.1, the peak of the graph of Infected *I(t)* increases while susceptible and recovered decreases (***Fig. 5-7***).

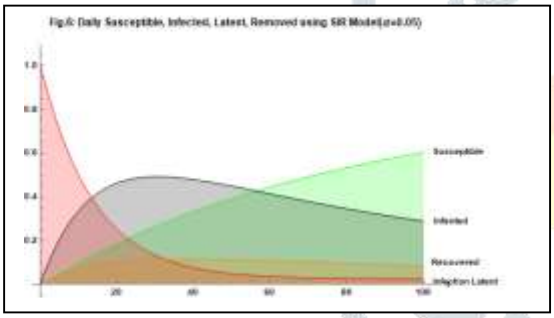


Fig.6: Daily Susceptible, Infected, Latent, Removed using SIR Model(α=0.05)

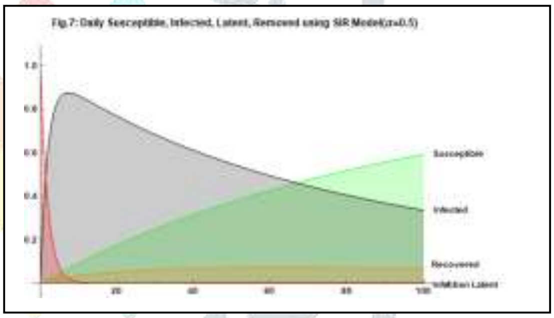
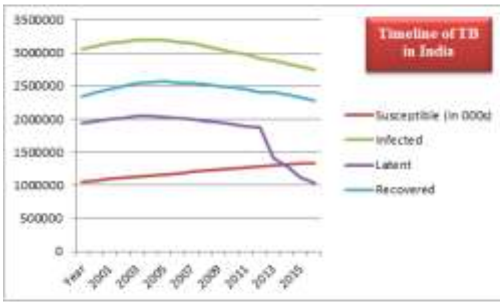


Fig.7: Daily Susceptible, Infected, Latent, Removed using SIR Model(α=0.5)

5. Conclusion

This study presents a simple yet realistic deterministic model for the transmission dynamics of tuberculosis. In contrast to many tuberculosis models in the literature, we have included the compartment latent (infection). The latent (infection) category is of particular importance in modelling tuberculosis as it remains latent or even after treatment, the virus may remain inactive in the body. The individuals who seek medical intervention and those who recover from active tuberculosis will move to the susceptible compartment. The statistics for the latent (infected) patient is not available as it remains unidentified. The recovery parameters also give an idea of failure in treating both active tuberculosis and latent tuberculosis. We have simulated both the recovery from the latent and infected compartment. We have established that by identifying the latently infected patients through diagnostic tests and treating them before they could become infectious will not only help in recovery but also the population of infected will reduce, consequently the spread will reduce being airborne contagious disease. Since there is no permanent immunity to tuberculosis and the recovered can still lose their immunity and become susceptible again therefore we have considered this factor [8]. This simplistic model indicates that the number of infections rises resulting in endemic and is found to be globally asymptotically stable **(*Fig. 8*).** (In the data [12], the high incidence rate of TB is assumed to be the total infected including latent infected.



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