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Modeling the Transmission Dynamics of Tuberculosis in Humans

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Abstract

Tuberculosis (TB) is a major threat to human health particularly in most of developing countries. In this article, we formulate and analyze a deterministic model for the transmission dynamics of pulmonary and extra-pulmonary tuberculosis. The next generation method is employed to find the basic reproduction number R_0 which helps to determine whether TB clears or persists in the human population. Global stability of model equilibria is done through Lyapunov functions whereas the normalized forward sensitivity index method is adopted to determine parameters that drive tuberculosis. Analysis shows that both TB free and endemic equilibria exist. The TB free equilibrium is globally asymptotically stable whenever the basic reproduction number $R_0 < 1$ whereas the endemic equilibrium is globally asymptotically stable whenever $R_0 > 1$. Sensitivity analysis shows that the TB infection rate, the fraction of individuals who progress to pulmonary tuberculosis and its induced death drive TB. Numerical results indicate that when there are no interventions, susceptible humans decline significantly with time until when they are attracted to the steady state whereas latently infected, pulmonary and extra-pulmonary TB individuals increase until when they settle at the equilibrium states supporting the analytical results for existence of the endemic equilibrium. In light of these findings, we recommend treating humans infected with pulmonary TB who are carriers of the disease.

Keywords: Tuberculosis; Basic reproduction number; Sensitivity analysis; Lyapunov function; Global stability

Introduction

Tuberculosis (TB) is an airborne disease caused by *Mycobacterium tuberculosis* bacteria. Humans contract TB through breathing in tuberculosis germs released in the air by an infected person during coughing, sneezing, speaking or singing (Lopes et al. 2014). There are two forms of TB, namely pulmonary tuberculosis and extra-pulmonary tuberculosis. Extra-pulmonary TB happens when *Mycobacterium tuberculosis* germs infect organs other than the lungs, whereas pulmonary TB arises when the bacteria infect the lungs. TB occurs in two different stages which are latent TB and active TB. Usually, latent TB individuals harbor the *Mycobacterium tuberculosis* germs, but they are not contagious (WHO, 2023). Active tuberculosis arises when TB germs evade the immune system and start growing within the human body (Marino et al., 2015). Though individuals with weak immunity get active TB immediately after infection, those with strong immunity acquire active TB later when their immune systems weaken (Lopes et al. 2014). Symptoms of TB include fatigue or weakness, weight loss, fever, chills, loss of appetite and night sweats (Halim 2013).

Despite the fact that TB has been controlled to some extent, the disease still poses a threat to human health, particularly in many underdeveloped countries. Tuberculosis ranks as the ninth most common cause of death worldwide. For instance, in 2016 a total of 10.4 million individuals, 2.5 million of whom were African, contracted tuberculosis. Globally, 1.7 million people died from TB in the same year, with 417,000 deaths occurring in Africa (Floyd et al., 2018). In 2021, the World Health Organization categorized Tanzania to be among 30 high-burden countries for TB whereby approximately 13,300 TB new cases and 26,800 deaths occurred in 2019 (WHO 2023)**.** Despite the presence of various interventions such as treatment of infected individuals, vaccination, patient education, financial and psychological support to patients with tuberculosis, TB remains a major challenge to human health particularly in developing countries due to the existence of multidrug resistance, delay in tuberculosis detection, undernourishment, HIV infection, alcohol use, smoking and diabetes mellitus (WHO 2023). Therefore, to design effective TB control strategies, it is necessary to understand how TB is transmitted.

Mathematical modeling has proven to be an effective tool in the study of infectious diseases transmission dynamics. Numerous mathematical models have been formulated over time to investigate TB dynamics. Nonetheless, most of them failed to take into account the two types of tuberculosis: pulmonary and extra-pulmonary TB. Therefore, this work attempts to study and analyze a mathematical model for transmission dynamics of both extra-pulmonary and pulmonary tuberculosis, and identify the factors that contribute to the spread of tuberculosis disease.

Materials and Methods

Mathematical Model and Analysis

In this section, we formulate and analyze a basic mathematical model for transmission dynamics of pulmonary and extra-pulmonary tuberculosis based on the work by Fatima et al. (2020) and Herrera et al., (2013). The study of Fatima et al. (2020) considered standard incidence rate, latent TB stage and immunity status of individuals though did not consider two types of TB whereas Herrera et al., (2013) considered human infection due to mass action principle, endogenous TB reactivation and exogenous reinfection. The human population is classified into susceptible S, latently infected L, infectious I and non-infectious N individuals. Individuals with pulmonary tuberculosis (TB) belong to the infectious class I, while individuals with extra-pulmonary TB belong to the non-infectious class N. The variable H conventionally represents the total human population where $H = S + L + I + N$.

Susceptible humans are recruited through birth at a rate r and contract tuberculosis (TB) at a rate $\lambda = \frac{\beta I}{H}$ through interaction with infected individuals where β is the infection rate. Following infection, individuals progress into latent, pulmonary or extra-pulmonary TB. A proportion α of weak immunity individuals acquires either pulmonary or extra-pulmonary TB whereas 1-α remain latently infected. Parameter δ is the fraction of individuals who contract pulmonary TB shortly after infection, whereas 1-δ represents the proportion of individuals who contract extra-pulmonary TB. The rate at which individuals with latent tuberculosis progress into pulmonary or extra-pulmonary TB as a result of endogenous reactivation is represented by parameter τ. The percentage of latently infected humans who develop into pulmonary tuberculosis is denoted by η, while the remaining percentage 1-η progresses to extra-pulmonary TB. Regardless of their status, all humans die naturally at a rate μ, whereas those with extra-pulmonary and pulmonary TB have extra TB-related mortality rates ψ and σ, respectively. When formulating the model, we take into account the standard incidence rate and make the assumption that there is no migration. Moreover, it is assumed that human recruitment into the susceptible compartment is constant through birth. Furthermore, exogenous reinfection is not taken into consideration and individuals with weak immunity are not regarded to undergo

the latent stage. Figure 1 summarizes the model flow chart for the dynamics of TB in humans whereas Table 1 provides descriptions of the model parameters. Taking into account the model assumptions and descriptions, a mathematical model for the transmission dynamics of TB is given as:

$$\begin{aligned}
\frac{dS}{dt} &= r - (\lambda + \mu)S, \\
\frac{dL}{dt} &= \lambda S - (\tau + \mu)L, \qquad (1) \\
\frac{dI}{dt} &= \lambda S + \tau\eta L - (\mu + \psi)I, \\
\frac{dN}{dt} &= \lambda S + \tau(1-\eta)L - (\mu + \sigma)N,
\end{aligned}$$

subject to initial conditions: $S > 0; L \geq 0, I \geq 0, N \geq 0$ where $\lambda = \frac{\beta I}{H}$.

Table 1: Description of model parameters

Parameter	Description
r	Human recruitment rate.
β	Infection rate of susceptible individuals.
α	Fraction of individuals that progress to pulmonary and extra-pulmonary TB.
δ	Percentage of humans who get pulmonary TB soon after infection
τ	Latent TB progression rate to pulmonary or extrapulmonary TB.
η	Fraction of latent TB individuals who develop into pulmonary TB.
μ	Human natural death rate.
σ	Extra-pulmonary TB induced death rate.
ψ	Pulmonary TB induced death rate.

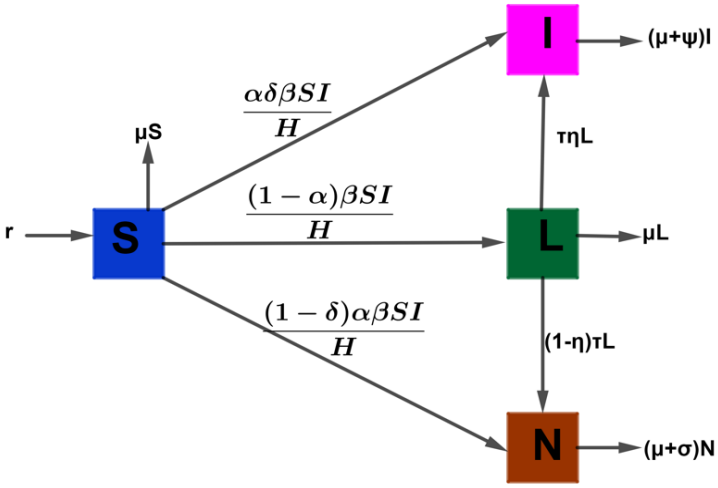

Figure 1: The flow chart illustrating TB transmission dynamics

Positivity and Boundedness of Model Solutions

It is important to demonstrate that the model solutions are positive and bounded for the model system (1) to be well-posed and epidemiologically significant.

Positivity of Model Solutions

To prove the positivity of model solutions, we first establish the following theorem.

Theorem 1: Let the initial conditions for the model system (1) be $S(0) > 0$; $L(0) \geq 0$; $I(0) \geq 0$ and $N(0) \geq 0$, then the solutions of the model system (1) with positive initial

conditions will remain non-negative for all $t \geq 0$.

Proof: Let $t_1 = sup\{t > 0 : S > 0, L > 0, I > 0, N > 0 \epsilon [0, t]\}$ so that $t_1 > 0$, then considering the equation for the susceptible population in the model system (1), we have:

$\frac{dS}{dt} = r - \lambda S - \mu S,$

$\Longrightarrow \frac{dS}{dt} \geq -(\lambda + \mu)S.$

Separation of variables leads to:

$\frac{dS}{S} \geq -(\lambda + \mu)dt.$

Integrating and using the initial condition, we get:

$S(t) \geq S(0)exp - \int_0^t (\lambda + \mu)ds \geq 0.$ (2)

Considering the latently infected individuals' equation in the model system (1), we have:

$\frac{dL}{dt} = (1 - \alpha)\lambda S - (\tau - \mu)L,$

$\Longrightarrow \frac{dL}{dt} \geq -(\tau + \mu)\mathrm{L}.$

Separation of variables leads to:

$\frac{dL}{L} \geq -(\tau + \mu)dt.$

Integrating and using the initial condition, we arrive at:

$L(t) \geq L(0)exp - \int_0^t (\tau + \mu)ds \geq 0.$ (3)

Using the same approach for the rest of system (1) model equations, it can be shown that:

$I(t) \geq I(0)\, exp\,[-(\mu + \psi)t]$ and $N(t) \geq N(0)\, exp[-(\sigma + \mu)t]$.

Therefore, for all non-negative initial conditions, all solutions of model system (1) will remain positive.

Boundedness of Model Solutions

Defining $H = S + L + I + N$ as conventionally the total human population, we can show that the model solutions are boundedness. Thus:

$\frac{dH}{dt} = \frac{dS}{dt} + \frac{dL}{dt} + \frac{dI}{dt} + \frac{dN}{dt}$ (4)

Substituting the equations of the model system (1) into equation (4) we obtain:

$\frac{dH}{dt} = \mathrm{r} - \mu\mathrm{H} - \psi\mathrm{I} - \sigma\mathrm{N},$

$\Longrightarrow \frac{dH}{dt} + \mu\mathrm{H} = \mathrm{r} - \psi\mathrm{I} - \sigma\mathrm{N},$

$\Longrightarrow \frac{dH}{dt} + \mu H \leq r.$ (5)

Equation (5) is a first order linear differential equation whose integrating factor is $e^{-\mu t}$.

Solving equation (5) and using the initial conditions, we get:

$H(t) \leq \frac{r}{\mu} + (H(0) - \frac{r}{\mu})e^{-\mu t}$

Applying limit as $t \to \infty$, it can be observed that:

$\lim_{t \to \infty} H(t) \leq \frac{r}{\mu}.$

Therefore, we can analyze the model system (1) since its solutions are positive bounded in the region $\Omega = \{S, L, I, N\} \in \mathbb{R}_+^4$.

Model Analysis

The TB Free Equilibrium Point

A steady state solution where there is no TB in the population is known as the TB free equilibrium point. To get the TB free equilibrium point, we set the right-hand side of the equations in the model system (1) equal to zero and solve for *S* when *L*=*I*=*N*=0. As a result, the TB free equilibrium point T_0 of model system (1) is $T_0(S^0, L^0, I^0, N^0) = (\frac{r}{\mu}, 0,0,0)$.

Basic Reproduction Number

The basic reproduction number R_0 is the number of secondary cases that may occur when one infectious individual is introduced in a full susceptible population (Diekmann et al., 1990). We use the next generation matrix approach to determine the basic reproduction number as applied in Diekmann et al., (1990). Let F_i represent the rates at which new infection emerge in the infected compartments i and V_i be the rates at which infected individuals move into and out of the compartments i, such that:

$$F_i = \begin{bmatrix} \frac{(1-\alpha)\beta SI}{H} \\ \frac{\alpha\delta\beta SI}{H} \\ \frac{(1-\delta)\alpha\beta SI}{H} \end{bmatrix} \text{ and}$$

$$V_i = \begin{bmatrix} (\tau + \mu)L \\ -\tau\eta L + (\mu + \psi)I \\ -\tau(1-\eta)L + (\sigma + \mu)I \end{bmatrix},$$

$$R_0 = \left(\frac{\partial F_i}{\partial y_j}(T_0)\right) \times \left(\frac{\partial V_i}{\partial y_j}(T_0)\right)^{-1} = \mathrm{FV}^{-1},$$

where y_j are the infected classes in the model system (1) and T_0 is the TB free equilibrium of model system (1). Therefore, the matrices F and V at TB free equilibrium are given as:

$$F = \begin{bmatrix} 0 & (1-\alpha)\beta & 0 \\ 0 & \alpha\delta\beta & 0 \\ 0 & \alpha(1-\delta)\beta & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} \tau + \mu & 0 & 0 \\ -\eta\tau & \mu + \psi & 0 \\ -(1-\eta)\tau & 0 & \mu + \sigma \end{bmatrix}.$$

The next generation matrix $FV^{-1} = \begin{bmatrix} \frac{(1-\alpha)\tau\beta\eta}{(\tau+\mu)(\mu+\psi)} & \frac{(1-\alpha)\beta}{(\mu+\psi)} & 0 \\ \frac{\tau\beta\eta\alpha\delta}{(\tau+\mu)(\mu+\psi)} & \frac{\alpha\delta\beta}{(\mu+\psi)} & 0 \\ \frac{(1-\delta)\tau\beta\eta\alpha}{(\tau+\mu)(\mu+\psi)} & \frac{(1-\delta)\alpha\beta\mu}{(\mu+\psi)} & 0 \end{bmatrix}.$

The basic reproduction number R_0 is the largest eigenvalue of the next generation matrix FV^{-1} denoted by $R_0 = \rho(FV^{-1})$. Therefore, the basic reproduction number R_0 is given by:

$$R_0 = \frac{\alpha\delta\beta(\tau+\mu)+(1-\alpha)\eta\tau\beta}{(\tau+\mu)(\mu+\psi)}. \quad (6)$$

Global Stability of TB Free Equilibrium Point

Theorem 4: The TB free equilibrium point T_0 of the model system (1) is globally asymptotically stable whenever $R_0 < 1$.

Proof: To prove the Theorem 4, consider the Lyapunov function:

$$V = \frac{\eta\tau L}{(\mu+\psi)(\tau+\mu)} + \frac{I}{\mu+\psi}.$$

$$\Rightarrow \frac{dV}{dt} = \left(\frac{\eta\tau L}{(\mu+\psi)(\tau+\mu)}\right)\frac{dL}{dt} + \left(\frac{I}{\mu+\psi}\right)\frac{dI}{dt}. \quad (9)$$

Substituting expressions for $\frac{dL}{dt}$ and $\frac{dI}{dt}$ from the model system (1) into equation (9), we have:

$$\frac{dV}{dt} = \left(\frac{\eta\tau}{(\mu+\psi)(\tau+\mu)}\right)\left(\frac{(1-\alpha)\beta SI}{H} - (\tau+\mu)L\right) + \left(\frac{1}{\mu+\psi}\right)\left(\frac{\alpha\beta\delta SI}{H} + \eta\tau L - (\mu+\psi)I\right),$$

$$\Rightarrow \frac{dV}{dt} = \frac{\eta\tau(1-\alpha)\beta SI}{(\mu+\psi)(\tau+\mu)H} - \frac{\eta\tau(\tau+\mu)L}{(\mu+\psi)(\tau+\mu)} + \frac{\alpha\beta\delta SI}{(\mu+\psi)H} + \frac{\eta\tau L}{\mu+\psi} - \frac{(\mu+\psi)I}{\mu+\psi},$$

$$\Rightarrow \frac{dV}{dt} = \frac{\eta\tau(1-\alpha)\beta SI}{(\mu+\psi)(\tau+\mu)H} - \frac{\eta\tau L}{(\mu+\psi)} + \frac{\alpha\beta\delta SI}{(\mu+\psi)H} + \frac{\eta\tau L}{\mu+\psi} - I,$$

$$\Rightarrow \frac{dV}{dt} = \left(\frac{\eta\tau(1-\alpha)\beta S}{(\mu+\psi)(\tau+\mu)H} + \frac{\alpha\beta\delta S}{(\mu+\psi)H} - 1\right)I.$$

At disease free equilibrium point $H = S$.

$$\Rightarrow \frac{dV}{dt} = \left(\frac{\eta\tau(1-\alpha)\beta}{(\mu+\psi)(\tau+\mu)} + \frac{\alpha\beta\delta}{(\mu+\psi)} - 1\right)I,$$

$$\Rightarrow \frac{dV}{dt} = (R_0 - 1)I.$$

Since all the model parameters are non-negative, it follows that $\frac{dV}{dt} \leq 0$ if $R_0 \leq 1$ and $I > 0$, whereas $\frac{dV}{dt} = 0$ if $I = 0$ or $R_0 = 1$. Therefore, V is Lyapunov function on D and the largest compact invariant set $(S, L, I, N) \in \Omega$ is the singleton TB free equilibrium T_0. Thus, the TB free equilibrium point is globally asymptotically stable when $R_0 < 1$.

Sensitivity Analysis

The normalized forward sensitivity index method, as described in Chitnis *et al*., (2008), is used to derive sensitivity indices. If Φ is a parameter in the basic reproduction number R_0, then its sensitivity index is given by $\Gamma_{\Phi}^{R_0} = \frac{\partial R_0}{\partial \Phi} \times \frac{\Phi}{R_0}$. Using parameter values in Table 2, we obtain the sensitivity indices of model parameters as shown in Figure 2. Using this approach, it can be shown that the sensitivity indices of parameters β, μ, α, δ, τ, η and ψ are respectively .0000, -0.4581, 0.5353, 0.8606, 0.0676, 0.1394 and -0.6094 as shown graphically in Figure 2. Figure 2 shows that the parameters most sensitive to tuberculosis (TB) transmission are the rate of tuberculosis infection in humans (β), the proportion of susceptible humans who develop pulmonary TB (δ), and the pulmonary TB-induced death (ψ). The positive sign of the sensitivity index indicates that increasing a given parameter value while keeping other parameter values constant leads to the increase in average number of secondary infection whereas the negative sign shows that increasing the parameter value reduces the average number of secondary infections. For example, as the parameter α with sensitivity index $+0.5353$ is increased by 10%, this leads to the increase of the basic reproduction number by 5.35%. Similarly, as the parameter ψ with sensitivity index -0.6094 is increased by 10%, the basic production number decreases by 6.09%.

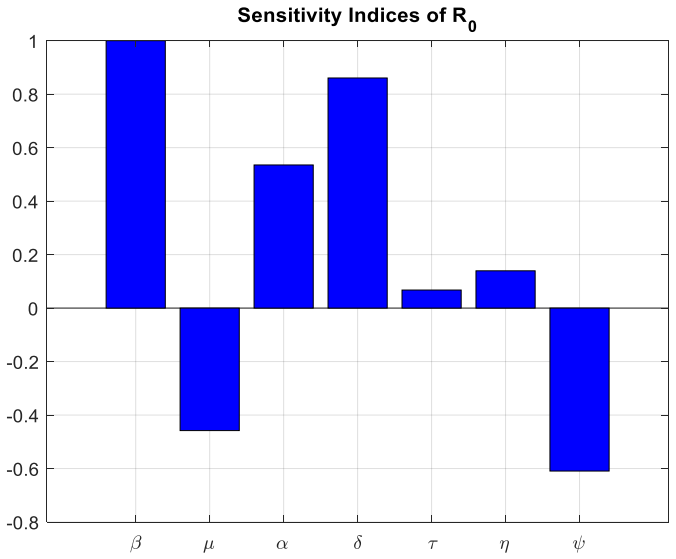

Figure 2: Sensitivity indices of parameters in R_0

Table 2: Parameter values

Parameter	Value	Source
μ	0.0141	Mwasunda et al., 2023
δ	0.75	Lopes et al., 2014
τ	0.015	Chong et al., 2019
ψ	0.022	Hickson et al., 2012
α	0.7	Herrera et al., 2013
η	0.55	Assumed
r	2	Bowong et al., 2010
σ	0.0015	Assumed
β	0.75	Assumed

Endemic Equilibrium Point

When TB persists in the human population, we obtain the endemic equilibrium point. The endemic equilibrium is obtained by setting the right-hand side of each equation of the model system (1) equal to zero and solving for the model variables S^*, L^*, I^* and N^*in term of force of infection λ. Thus, the endemic equilibrium is given as $T^* = (S^*, L^*, I^*, N^*)$ where:

$S^* = \frac{r}{\lambda+\mu}$, $I^* = \frac{r\alpha\lambda\delta(\mu+\tau)+(1-\alpha)\tau\eta\lambda r}{(\tau+\mu)(\lambda+\mu)(\mu+\psi)}$, $L^* = \frac{(1-\alpha)\lambda r}{(\tau+\mu)(\lambda+\mu)}$, $N^* = \frac{(1-\delta)(\tau+\mu)\alpha\lambda r+(1-\eta)(1-\alpha)\tau\lambda r}{(\tau+\mu)(\lambda+\mu)(\mu+\sigma)}$.

Since $\lambda = \frac{\beta I}{H}$ and $H = S + L + I + N$, it can be shown that:

$\lambda(A\lambda + B) = 0, \quad (12)$

where

$A = \mu^2 + \psi\Big(\sigma(1-\alpha) + \tau\Big(1 - \big(\alpha\delta + \eta(1-\alpha)\big)\Big)\Big) + \mu\Big(\sigma\big(1 + (1-\delta)\big) + \tau + \psi(1-\alpha\delta)\Big) + \sigma\alpha\delta\tau + \sigma\eta\tau(1-\alpha) \quad (13)$

$B = (\mu+\psi)(\tau+\mu)(\mu+\sigma) - \beta(\mu+\sigma)\big(\alpha\delta(\tau+\mu) + \eta\tau(1-\alpha)\big) \quad (14)$

Solving (12), we obtain $\lambda = 0$ and $A\lambda + B = 0$. When $\lambda = 0$, we have TB-free equilibrium; nevertheless, when $A\lambda + B = 0$, then TB persists in the human population. When we solve for λ if $A\lambda + B = 0$ we get:

$$\lambda = -\frac{B}{A}. \qquad (15)$$

Substituting the value of B into equation (15), we obtain:

$$\lambda = \frac{1}{A}(\mu + \psi)(\tau + \mu)(\mu + \sigma)(R_0 - 1). \qquad (16)$$

Therefore, the model system (1) has a unique endemic equilibrium point which is globally asymptotically stable when the basic reproduction number $R_0 > 1$. We summarize this result in Theorem 5.

Theorem 5: The model system(1) has a unique endemic equilibrium E^* whenever $R_0 > 1$.

Global Stability of Endemic Equilibrium Point

We employ the methodology applied by Mwasunda et al. (2023) to prove the global stability of the endemic equilibrium point. Consider the logarithmic Lyapunov function:

$$\mathcal{L} = \left(S - S^* - S^* \ln\left(\frac{S^*}{S}\right)\right) + \left(L - L^* - L^* \ln\left(\frac{L^*}{L}\right)\right) + \left(I - I^* - I^* \ln\left(\frac{I^*}{I}\right)\right) + \left(N - N^* - N^* \ln\left(\frac{N^*}{N}\right)\right)$$

$$\Rightarrow \frac{d\mathcal{L}}{dt} = \left(\frac{S-S^*}{S}\right)\frac{dS}{dt} + \left(\frac{L-L^*}{L}\right)\frac{dL}{dt} + \left(\frac{I-I^*}{I}\right)\frac{dI}{dt} + \left(\frac{N-N}{N}\right)\frac{dN}{dt}. \qquad (17)$$

Substituting $\frac{dS}{dt}, \frac{dL}{dt}, \frac{dI}{dt}$ and $\frac{dN}{dt}$ expressions from the model system (1) into equation (17),

$$\Rightarrow \frac{d\mathcal{L}}{dt} = \left(\frac{S-S^*}{S}\right)(r - \lambda S - \mu S) + \left(\frac{L-L^*}{L}\right)\left((1-\alpha)\lambda S - (\tau + \mu)L\right) + \left(\frac{I-I^*}{I}\right)(\alpha\delta\lambda S + \eta\tau L - (\mu + \psi)I) + \left(\frac{N-N^*}{N}\right)\left((1-\delta)\lambda\alpha S + (1-\eta)\tau L - (\mu + \sigma)N\right).$$

At the endemic equilibrium point, we have:

$$\frac{d\mathcal{L}}{dt} = \left(\frac{S-S^*}{S}\right)(\lambda S^* + \mu S^* - \lambda S - \mu S) + \left(\frac{L-L^*}{L}\right)\left((\tau + \mu)L^* - (\tau + \mu)L\right) + \left(\frac{I-I^*}{I}\right)\left((\mu + \psi)I^* - (\mu + \psi)I\right) + \left(\frac{N-N}{N}\right)\left((\mu + \sigma)N^* - (\mu + \sigma)N\right),$$

$$\Rightarrow \frac{d\mathcal{L}}{dt} = (\lambda + \mu)S^* - (\lambda + \mu)S - \frac{(\lambda+\mu)S^{*2}}{s} + (\lambda + \mu)S^* + (\tau + \mu)L^* - (\tau + \mu)L - \frac{(\tau+\mu)L^{*2}}{L} + (\tau + \mu)L^* + (\mu + \psi)I^* - (\mu + \psi)I - \frac{(\mu+\psi)I^{*2}}{I} + (\mu + \psi)I^* + (\mu + \sigma)N^* - (\mu + \sigma)N - \frac{(\mu+\sigma)N^{*2}}{N} + (\mu + \sigma)N^*,$$

$$\Rightarrow \frac{d\mathcal{L}}{dt} = (\lambda + \mu)S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + (\tau + \mu)L^*\left(2 - \frac{L}{L^*} - \frac{L^*}{L}\right) + (\mu + \psi)I^*\left(2 - \frac{I}{I^*} - \frac{I^*}{I}\right) + (\mu + \sigma)N^*\left(2 - \frac{N}{N^*} - \frac{N^*}{N}\right). \qquad (18)$$

Since the arithmetic mean exceeds the geometric mean value, it follows that:

$$\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) \leq 0, \left(2 - \frac{L}{L^*} - \frac{L^*}{L}\right) \leq 0, \left(2 - \frac{I}{I^*} - \frac{I^*}{I}\right) \leq 0, \left(2 - \frac{N}{N^*} - \frac{N^*}{N}\right) \leq 0.$$

Since all model parameters are positive, then $\frac{d\mathcal{L}}{dt} \leq 0$ for $R_0 > 1$. Hence by LaSalle's invariance principle (LaSalle 1976), every solution of the model system (1) approaches the endemic equilibrium point T^* as $t \to \infty$ whenever $R_0 > 1$.

Results and Discussion

Simulation of Model System

In this section, we perform numerical simulation of model the model system (1) using parameter values in Table 2 and briefly discuss the results obtained. It can be seen from Figure 3 that susceptible humans decline significantly within the first 20 years following infection and then settle to a steady state whereby only a small proportion remains uninfected. This trend has consequently resulted to an increase in the number of latently infected humans, individuals with pulmonary tuberculosis and individuals with extra-pulmonary tuberculosis whereby these populations grow with time until when they attain their steady state after the 20th year. These results show that TB will continue to persist in the human population as long as no control is taken to control the disease.

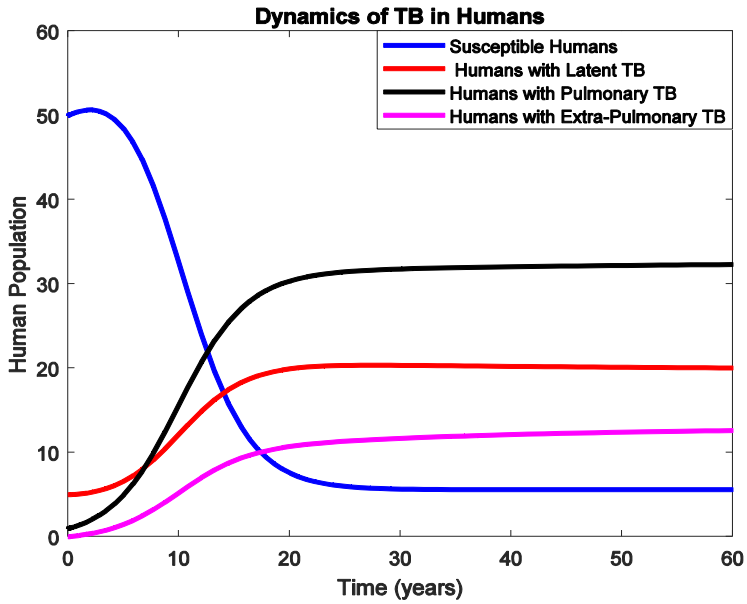

Figure 3: Dynamics of tuberculosis in humans when there is no any control measure

Impact of Varying the Most Sensitive Parameters on the Dynamics of TB

In this section, we carry out simulation of the model system (1) by varying the value of most sensitive parameter so as to study their contribution on the transmission of tuberculosis.

Impact of Varying the Probability of Infection on TB Dynamics

Figure 4 (a) shows that the susceptible population decreases with the increase in the infection rate β. This is the case since the increase in the infection rate increases the chance of susceptible individuals to acquire TB, leading to the decline of the susceptible population. On the other hand, Figures 4(b), (c), and (d) indicate that the latently infected individuals, individuals with pulmonary and extra-pulmonary tuberculosis increase with the increase in the infection β. These results are in correspondence with the disease dynamics where susceptible humans decrease due to infection while other infectious classes increase with time when no intervention is taken to control the disease.

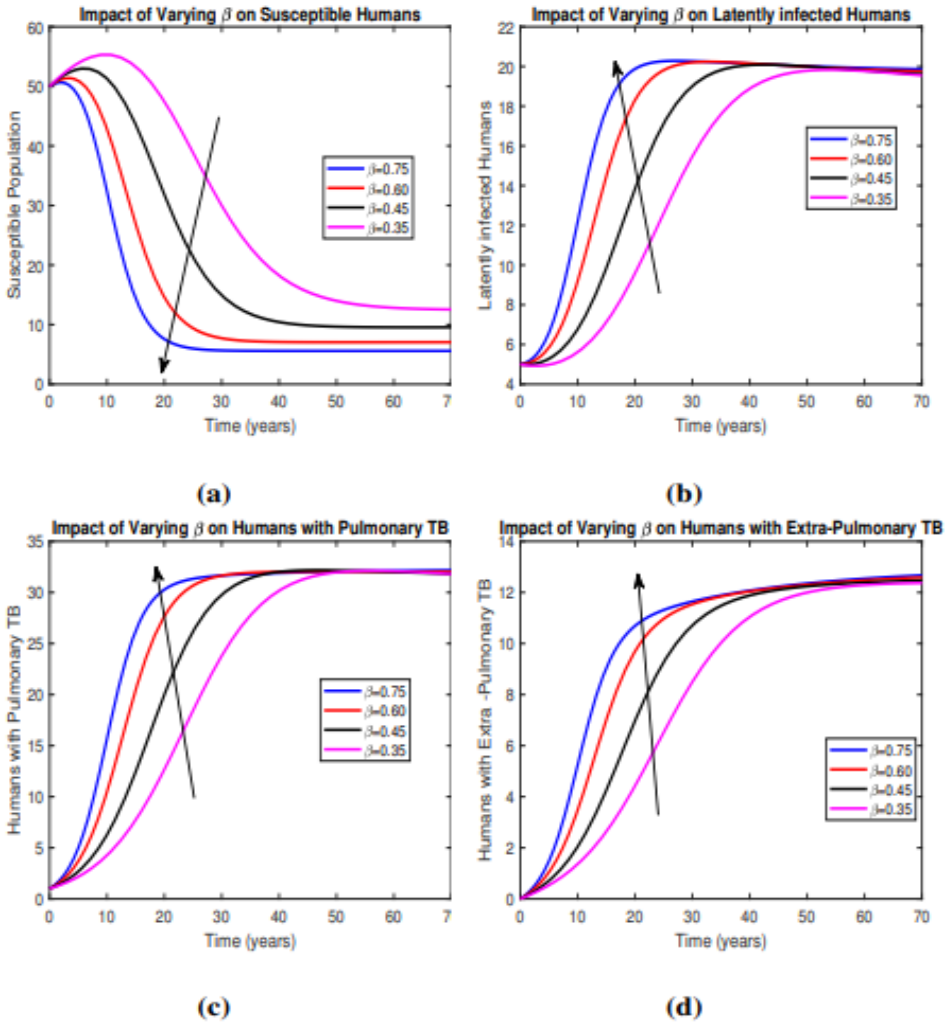

Figure 4: Impact of varying the probability of infection on TB dynamics

Impact of Varying the Proportion of Susceptible Humans who progress to Pulmonary TB

The results in Figure 5(c) show that humans with pulmonary tuberculosis increase with time as a result of an increase in the proportion of individuals δ that progress to pulmonary TB class affecting positively latently infected class as indicated in Figure 5(b). However, a different trend can be observed for susceptible humans and humans with extra-pulmonary TB in Figures 5 (a) and 5 (d) where there is a decrease in number of susceptible humans and individuals with extra-pulmonary TB. This is the case since increasing parameter δ reduces proportion of pulmonary TB individuals and increases pulmonary TB individuals leading to reducing susceptible population and increase in latently infected individuals.

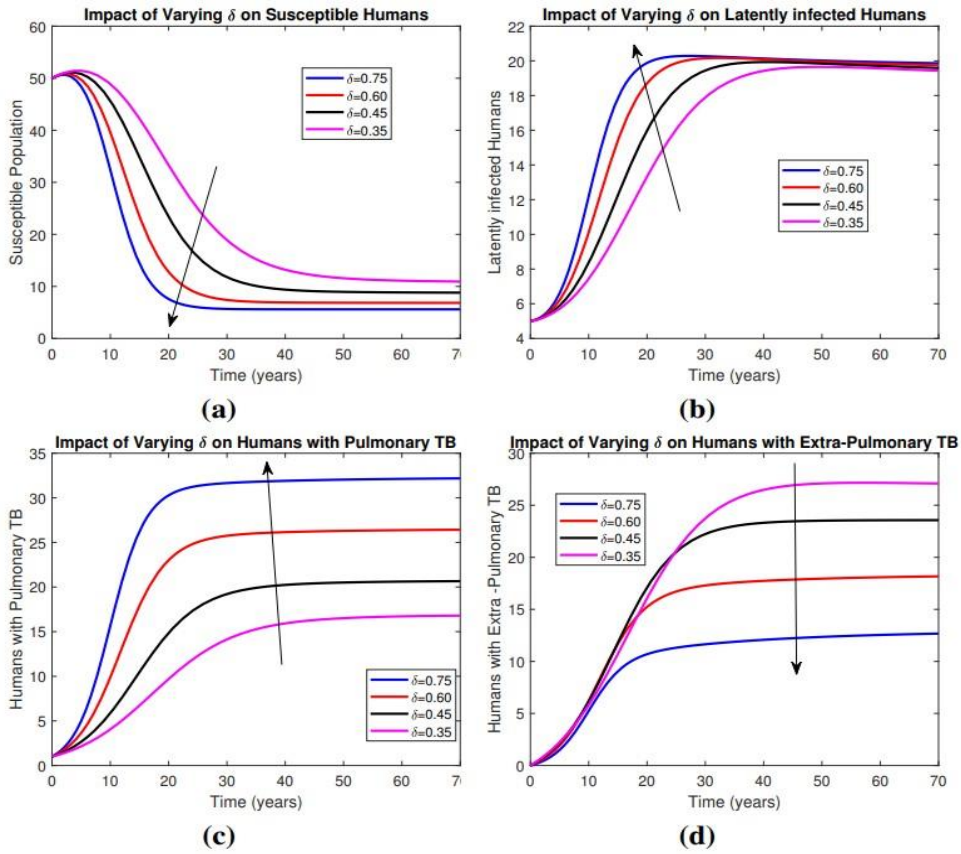

Figure 5: Impact of varying the proportion of susceptible humans who progress to pulmonary TB

Impact of Varying Pulmonary Disease-Induced Death on the Dynamics of TB

When more individuals with pulmonary TB die due to the disease, they reduce the chance for susceptible individuals to contract TB. This causes decline in a number of latently infected individuals, as well as individuals with pulmonary and extra-pulmonary TB as shown in Figures 6(b), (c), and (d). This consequently leads to an increase in a number of susceptible individuals as shown in Figure 5(a). However, it is not practical to let people die due to pulmonary TB-induced death ψ, rather than putting more efforts to save peoples' life. Thus, we recommend putting more efforts to treat individuals with pulmonary tuberculosis so as to control the transmission of TB.

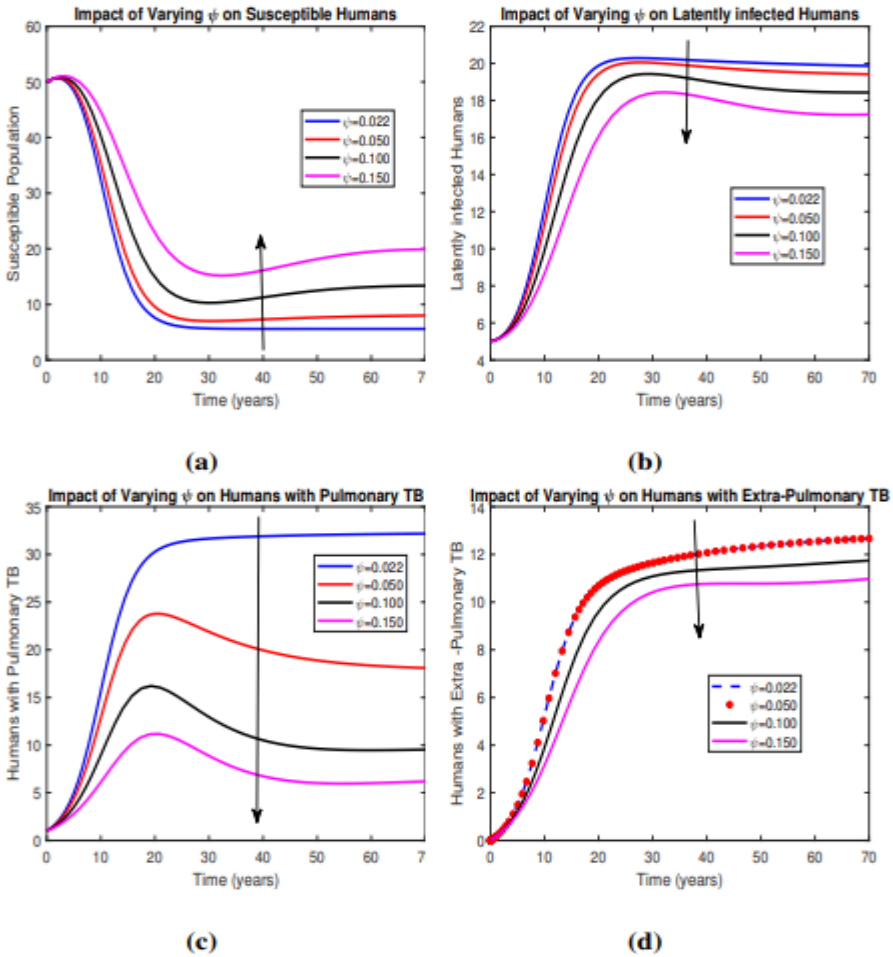

Figure 6: Impact of varying pulmonary disease induced death on the dynamics of TB

Conclusion

In this work, a mathematical model for transmission dynamics of both pulmonary and extra-pulmonary tuberculosis is formulated and analyzed to get insight on the disease's dynamics in human population. The basic reproduction number R_0 is computed through the next generation method. The TB free equilibrium is globally asymptotically stable when $R_0 < 1$ whereas the endemic equilibrium is globally asymptotically stable when $R_0 > 1$. Sensitivity analysis of parameters in the basic reproduction number R_0 is done using the forward normalized sensitivity index method. Results indicate that the probability of TB infection, the fraction of individuals who progress to pulmonary TB and pulmonary TB induced death influence TB disease. Thus to control TB, more effort is needed to reduce pulmonary TB individuals who are carriers of TB disease. Therefore, further research should focus on assessing the impact of treatment of individuals with pulmonary TB and vaccination of susceptible individual on TB control.

Declaration

The authors declare that they have no conflicts of interest upon publication of this work.

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