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A tuberculosis model with three infected classes

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Abstract

The dynamics of tuberculosis within a population cannot be adequately represented by a single infectious class. Therefore, this study develops a compartmental model encompassing latent, active, and drug-resistant populations to better capture tuberculosis dynamics in a community. Model analysis reveals that the disease-free equilibrium point is locally asymptotically stable when the basic reproduction number is below one. Moreover, the use of a suitable Lyapunov function demonstrates global asymptotic stability of the disease-free equilibrium point. An endemic equilibrium emerges when the basic reproduction number exceeds one. Sensitivity analysis is conducted for each parameter associated with the basic reproduction number, and optimal control analysis is employed to assess the impact of various control strategies on disease containment. Numerical simulations are conducted to supplement theoretical findings, illustrating the practical implications of the proposed control strategies.

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1. Introduction

Tuberculosis (TB), an airborne contagious bacterial infection primarily affecting the lungs, is caused by the bacterium M. Tuberculosis, which is transmitted through droplets expelled during activities such as sneezing and coughing. Its historical prevalence remains significant, with an estimated one-third of the global population carrying the infectious organism, particularly affecting regions with high rates of malnutrition, poverty, and HIV/AIDS, resulting in substantial morbidity and mortality, particularly in developing countries [1]. The emergence of multi-drug resistance poses additional challenges, making TB management increasingly difficult even in regions traditionally considered more equipped to handle it, such as Eastern Europe and Central Asia.

Given TB's complex natural history characterized by latent infection and slow disease progression, its modeling necessitates multiple stages for accurate analysis [2]. Various studies have explored mathematical models with multiple infected classes, demonstrating the disease's dynamics and potential control strategies [3–7]. For instance, Ojo et al. developed a mathematical model with six compartments to control TB epidemiology, while Ucakana et al. employed SIR, SEIR, and BSEIR models for parameter estimation in TB analysis, considering factors like vaccination and susceptibility [8, 9].

Das *et al.* investigated the transmission dynamics of TB

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with multiple reinfections, identifying conditions for backward bifurcation and establishing eradication thresholds, supported by numerical simulations [10]. Similarly, Mettle *et al.* [11] formulated an SEIR model specific to TB transmission dynamics in the Ashanti Region of Ghana, highlighting the efficacy of early treatment initiation during the exposed stage in curbing disease spread. Notably, the latent stage of TB infection plays a pivotal role, despite individuals not exhibiting symptoms or transmitting the disease; however, gradual weakening of the immune system during this stage may increase susceptibility to other infections like HIV [12, 13].

In this paper, we propose a mathematical model for TB transmission dynamics featuring three infected classes: latent, active, and drug-resistant, incorporating optimal control strategies focusing on prevention and early treatment during the latent stage. Acknowledging the latent stage's critical importance in TB management, despite its lack of direct disease transmission, underscores the need for comprehensive approaches to address TB's complex dynamics and associated challenges [14–17].

2. Model Description and Representation

The population is grouped into five segments: S denotes the susceptible population (individuals who are yet to be infected with TB); I_1 denotes latent population (individuals who are infected with TB but showing no symptoms); I_2 denotes the active infectious population (individuals who are infected and showing symptoms), I_3 denotes the drug resistant population (Individuals who do not recover after successful application of first line of treatment) and R denotes the recovered population (individuals who have been successfully treated).

Individuals in susceptible section are recruited at rate of Λ and there is reduction in the susceptible population through contact with active infectious and drug resistant individuals at rate β, which results in an increase in the latent class. The parameter $0 < \rho \leq 1$ is a modification factor which accounts for the reduced likelihood of the individuals in the active infection state to infect the susceptible population when compared to the individuals in the drug resistant state.

There is a reduction in the latent class as a result of effectiveness of early treatment at rate γ_1 and progression to active infectious stage or drug resistant stage at rate α_1 and α_2 respectively. There is a reduction by effective treatment at rate γ_2 in the active infectious class, progression at rate θ to drug resistant stage and death by TB at rate δ_1. Extensive treatment application in the drug resistant class and death by TB reduce the population at rate γ_3 and δ_2, respectively. Effective treatment from the three infected classes contribute to an increase in the recovered population and all compartments at rate μ experience natural death. The dynamical system described above is illustrated in Figure **??** and represented below by the following

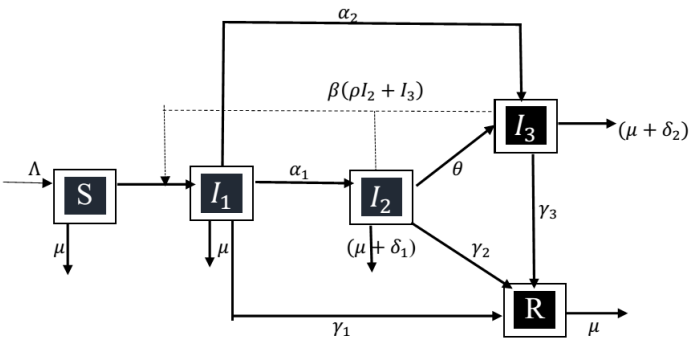

Figure 1: Flow diagram of the model.

differentials equations:

$$\frac{dS}{dt} = \Lambda - \beta S(\rho I_2 + I_3) - \mu S. \quad (1)$$

$$\frac{dI_1}{dt} = \beta S(\rho I_2 + I_3) - (\alpha_1 + \alpha_2 + \gamma_1 + \mu) I_1. \quad (2)$$

$$\frac{dI_2}{dt} = \alpha_1 I_1 - (\theta + \delta_1 + \gamma_2 + \mu) I_2. \quad (3)$$

$$\frac{dI_3}{dt} = \alpha_2 I_1 + \theta I_2 - (\gamma_3 + \delta_2 + \mu) I_3. \quad (4)$$

$$\frac{dR}{dt} = \gamma_1 I_1 + \gamma_2 I_2 + \gamma_3 I_3 - \mu R. \quad (5)$$

with initial conditions: $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, I_3(0) \geq 0, R(0) \geq 0$.

3. Results and Discussions

3.1. Invariant Region

This is done by obtaining the region Ω where the solution of the model is bounded and every solution that starts in Ω remains in Ω for all time $t \geq 0$

Theorem 3.1. *(Invariant region). All feasible solution of the system (1)-(5) with initial values: $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, I_3(0) \geq 0, R(0) \geq 0$ enters the region Ω represented by $\{S(t), I_1(t), I_2(t), I_3(t), R(t) \in \mathbb{R}^5_+ : N(0) \leq N(t) \leq \frac{\Lambda}{\mu}\}$ and are bounded.*

Proof: The total population is given by $N(t) = S(t) + I_1(t) + I_2(t) + I_3(t) + R(t)$. Hence,

$$\frac{dN}{dt} = \Lambda - \mu N - \delta_1 I_2 - \delta_2 I_3. \quad (6)$$

In the absence of disease induced death, Eq. (6) becomes

$$\frac{dN}{dt} \leq \Lambda - \mu N. \quad (7)$$

Solving equation (7) gives:

$$0 \leq N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}).$$

If $N(0) \leq \frac{\Lambda}{\mu}$, then $N(t) \leq \frac{\Lambda}{\mu}$ as $t \to \infty$. Hence,

$$N(0) \leq N(t) \leq \frac{\Lambda}{\mu}. \quad (8)$$

Table 1: Notation, description and values of parameters used.

Definition	Symbol	Value	Source
Recruitment term	Λ	0.6	Assumed
Rate of transmission	β	0.12	[10]
Natural death rate	μ	0.02041	Assumed
Transfer rate from latent to active infected stage	α_1	0.06	[10]
Transfer rate from latent to drug resistant stage	α_2	0.003	Assumed
Transfer rate from active to drug resistant stage	θ	0.470104	[15]
Modification factor	ρ	(0,1)	Variable
Treatment rate from latent infected class	γ_1	0.3	Assumed
Treatment rate from active infected class	γ_2	0.0575	[15]
Treatment rate from drug resistant stage	γ_3	0.1106456	[15]
TB death rate in active infected class	δ_1	0.01	[15]
TB death rate in drug resistant class	δ_2	0.0575	[15]

Thus, the feasible solution set of the model enters and remains in the region Ω. Hence, the model under consideration is epidemiologically and mathematically well posed. The model dynamics can therefore be sufficiently studied in Ω. Thus Ω is a positive invariant set.

3.2. Positivity of Solution

The initial condition of the system (1)-(5) is assumed to be nonnegative and the positivity of solution of the system shall be established.

Theorem 3.2. *(Positivity of Solution) The solutions $S(t), I_1(t), I_2(t), I_3(t), R(t)$ of (1)-(5) are nonnegative for $t \geq 0$ within the region Ω represented by $\{S(t), I_1(t), I_2(t), I_3(t), R(t) \in \mathbb{R}^5_+\}$ with initial values: $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0, I_3(0) \geq 0, R(0) \geq 0$.*

Proof: Solving (refeq1) gives:

$$\frac{dS}{dt} = \Lambda - \beta S(\rho I_2 + I_3) - \mu S \geq -\beta S(\rho I_2 + I_3) - \mu S,$$

$$\frac{dS}{dt} \geq -[\beta(\rho I_2 + I_3) - \mu]S,$$

$$\frac{dS}{S} \geq -[\beta(\rho I_2 + I_3) - \mu]dt,$$

$$\int \frac{dS}{S} \geq -\int [\beta(\rho I_2 + I_3) - \mu]dt,$$

Applying separation of variables method gives

$$S(t) \geq S(0)e^{-[\int_0^t Q d\tau + \mu t]} \geq 0,$$

where $Q = \beta(kI_1 + I_2)$.
Similar procedure can be used to show that $I_1(t) \geq 0, I_2(t) \geq 0, I_3(t) \geq 0, R(t) \geq 0$.
Hence, the solution of the model is positive.

3.3. Disease-free equilibrium

The disease-free equilibrium is obtained by equating (1)-(5) to zero such that $I_1 = I_2 = I_3 = 0$. It is given by

$$\pi_0 = (S^0, I_1^0, I_2^0, I_3^0, R^0) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0). \quad (9)$$

3.3.1. Basic Reproduction number

It is computed by using the method described in Refs. [18, 19]. The notation $\mathcal{F}$ represents the appearance of new infection while the notation $\mathcal{V}$ represents the transitional terms in the infected compartments as shown below:

$$\mathcal{F} = \begin{pmatrix} \beta S(\rho I_2 + I_3) \\ 0 \\ 0 \end{pmatrix},$$

$$\mathcal{V} = \begin{pmatrix} (\alpha_1 + \alpha_2 + \gamma_1 + \mu)I_1 \\ -\alpha_1 I_1 + (\theta + \delta_1 + \gamma_2 + \mu)I_2 \\ -\alpha_2 I_1 - \theta I_2 + (\gamma_3 + \delta_2 + \mu)I_3 \end{pmatrix}.$$

The linearized matrices F and V, computed at the disease-free equilibrium from above gives

$$F = \begin{pmatrix} 0 & \frac{\rho\beta\Lambda}{\mu} & \frac{\beta\Lambda}{\mu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} (\alpha_1 + \alpha_2 + \gamma_1 + \mu) & 0 & 0 \\ -\alpha_1 & (\theta + \delta_1 + \gamma_2 + \mu) & 0 \\ -\alpha_2 & -\theta & (\gamma_3 + \delta_2 + \mu) \end{pmatrix}.$$

The basic reproduction number R_0 is given by $\rho(FV^{-1})$ where ρ is the spectral radius. Thus,

$$R_0 = \frac{\beta\Lambda\{\alpha_1[\theta + \rho(\gamma_3 + \delta_2 + \mu)] + \alpha_2(\theta + \delta_1 + \gamma_2 + \mu)\}}{\mu(\alpha_1 + \alpha_2 + \gamma_1 + \mu)(\theta + \delta_1 + \gamma_2 + \mu)(\gamma_3 + \delta_2 + \mu)}. \quad (10)$$

3.3.2. Local stability of disease-free equilibrium

Theorem 3.3. *(Local stability of disease-free equilibrium). The disease-free equilibrium for the TB system under consideration is locally asymptotically stable if $R_0 < 1$ and unstable otherwise.*

Proof: We evaluate the Jacobian matrix of (1)-(5) at π_0 and it is given below:

$$\begin{pmatrix} -\mu & 0 & \frac{-\rho\beta\Lambda}{\mu} & \frac{-\beta\Lambda}{\mu} & 0 \\ 0 & -(\alpha_1 + \alpha_2 + \gamma_1 + \mu) & \frac{\rho\beta\Lambda}{\mu} & \frac{\beta\Lambda}{\mu} & 0 \\ 0 & \alpha_1 & -(\theta + \delta_1 + \gamma_2 + \mu) & 0 & 0 \\ 0 & \alpha_2 & \theta & -(\gamma_3 + \delta_2 + \mu) & 0 \\ 0 & \gamma_1 & \gamma_2 & \gamma_3 & -\mu \end{pmatrix}.$$

The eigenvalues of the Jacobian matrix are found to be $-\mu$ and $-\mu$. The remaining eigenvalues can be obtained from the matrix given below.

$$\begin{pmatrix} -(\alpha_1+\alpha_2+\gamma_1+\mu) & \frac{\rho\beta\Lambda}{\mu} & \frac{\beta\Lambda}{\mu} \\ \alpha_1 & -(\theta+\delta_1+\gamma_2+\mu) & 0 \\ \alpha_2 & \theta & -(\gamma_3+\delta_2+\mu). \end{pmatrix}$$

The characteristic equation is of the form:

$$p(\lambda) = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0.$$

where

$a_1 = (\alpha_1+\alpha_2+\gamma_1+\mu) + (\theta+\delta_1+\gamma_2+\mu) + (\gamma_3+\delta_2+\mu)$

$a_2 = (\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu) + (\alpha_1+\alpha_2+\gamma_1+\mu)(\gamma_3+\delta_2+\mu) + (\theta+\delta_1+\gamma_2+\mu)(\gamma_3+\delta_2+\mu) - \frac{(\rho\alpha_1+\alpha_2)\beta\Lambda}{\mu}$

$a_3 = (\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)(\gamma_3+\delta_2+\mu)(1-R_0)$

Applying Routh Hurwitz criterion gives $a_1 > 0, a_2 > 0$, and $a_1a_2 > a_3$.

Hence, the roots of the characteristic equation have a negative real part which shows that the disease-free equilibrium point is locally asymptotically stable if $R_0 < 1$.

3.4. Endemic equilibrium

It occurs when the disease cannot be eradicated in the population. It is obtained by setting (1)-(5) to zero.

Theorem 3.4. *(Existence of endemic equilibrium). The model (1)-(5) has an endemic equilibrium when $R_0 > 1$.*

Proof: We used the notation $E^* = (S^*, I_1^*, I_2^*, I_3^*, R^*)$ to denote the system's endemic equilibrium. The endemic equilibrium of the model (1)-(5) is given by

$$\begin{aligned}
S^* &= \frac{\Lambda}{\mu R_0}. \\
I_1^* &= \frac{\Lambda(R_0-1)}{R_0(\alpha_1+\alpha_2+\gamma_1+\mu)}. \\
I_2^* &= \frac{\alpha_1\Lambda(R_0-1)}{R_0(\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)}. \\
I_3^* &= \frac{[\alpha_2(\theta+\delta_1+\gamma_2+\mu)+\alpha_1\theta]\Lambda(R_0-1)}{R_0(\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)(\gamma_3+\delta_2+\mu)}. \\
R^* &= \frac{\Lambda(R_0-1)}{\mu R_0(\alpha_1+\alpha_2+\gamma_1+\mu)}(\alpha_1 + \frac{\alpha_1\gamma_2}{(\theta+\delta_1+\gamma_2+\mu)} + \\
&\quad \frac{[\alpha_2(\theta+\delta_1+\gamma_2+\mu)+\alpha_1\theta]}{(\theta+\delta_1+\gamma_2+\mu)(\gamma_3+\delta_2+\mu)}).
\end{aligned}$$

The implication of this situation epidemiologically is that tuberculosis is established in the population provided that $R_0 > 1$.

3.5. Global Stability

Here, we investigate the global asymptotic stability property of the disease-free equilibrium for the epidemic model.

Theorem 3.5. *(Global stability of disease-free equilibrium). The disease free equilibrium of the model (1)-(5) is globally asymptotically stable if $R_0 \leq 1$.*

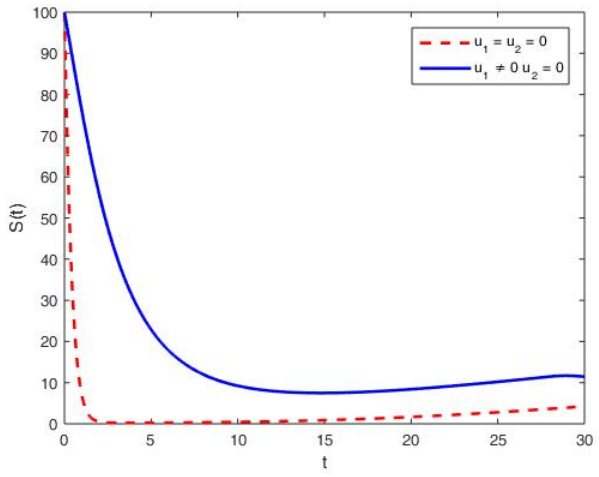

Figure 2: Numerical simulation of TB model showing effect of prevention on susceptible class

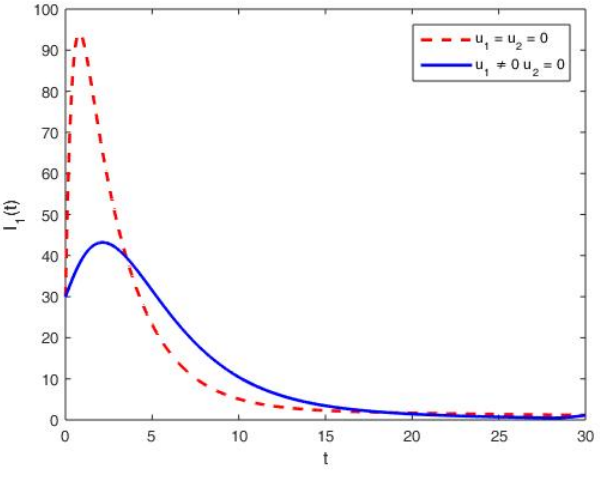

Figure 3: Numerical simulation of TB model showing effect of prevention on latent class

Proof: The global stability of the disease free equilibrium is proved using the Lyapunov function V defined below.

$$V = \frac{\alpha_2(\theta+\delta_1+\gamma_2+\mu)+\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]}{(\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)}I_1 + \frac{\theta+\rho(\gamma_3+\delta_2+\mu)}{(\theta+\delta_1+\gamma_2+\mu)}I_2 + I_3. \tag{11}$$

Differentiating both sides gives:

$$\dot{V} = \frac{\alpha_2(\theta+\delta_1+\gamma_2+\mu)+\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]}{(\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)}[\beta S(\rho I_2+I_3) - (\alpha_1+\alpha_2+\gamma_1+\mu)I_1] + \frac{\theta+\rho(\gamma_3+\delta_2+\mu)}{(\theta+\delta_1+\gamma_2+\mu)}(\alpha_1 I_1 - (\theta+\delta_1+\gamma_2+\mu)I_2) + \alpha_2 I_1 + \theta I_2 - (\gamma_3+\delta_2+\mu)I_3.$$

Simplifying gives

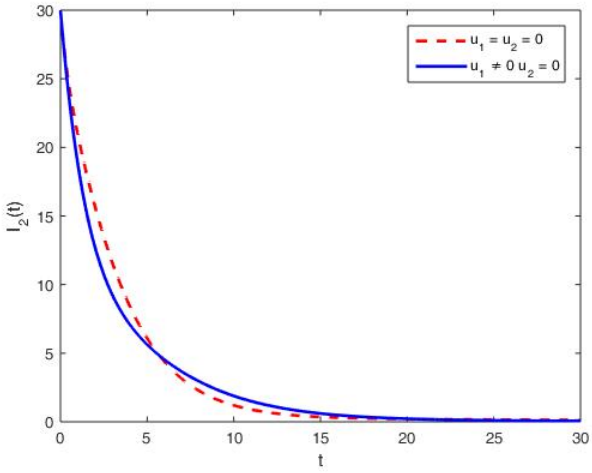

Figure 4: Numerical simulation of TB model showing effect of prevention on Active class

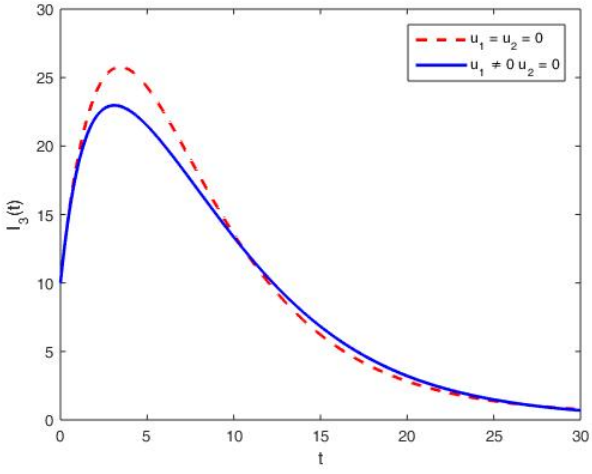

Figure 5: Numerical simulation of TB model showing effect of prevention on Drug resistant class

$$\dot{V} = \frac{\alpha_2(\theta+\delta_1+\gamma_2+\mu)+\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]}{(\alpha_1+\alpha_2+\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)}[\beta S(\rho I_2+I_3)] - (\gamma_3+\delta_2+\mu)(\rho I_2+I_3).$$

At $S = S_0 = \frac{\Lambda}{\mu}$,
$\dot{V} \leq (\gamma_3+\delta_2+\mu)(\rho I_2+I_3)[R_0-1]$.

Thus, $\dot{V} \leq 0$ if $R_0 \leq 1$ with equality if and only if $I_2 = I_3 = 0$. Every solution in with initial conditions in Ω as $t \to \infty$ approaches π_0 according to LaSalle's Invariance Principle [20].

3.6. Sensitivity Analysis

Sensitivity analysis on basic parameters is examined so as to quantify how each parameters contribute to the basic reproduction number. If a parameter p depends on X, the normalised

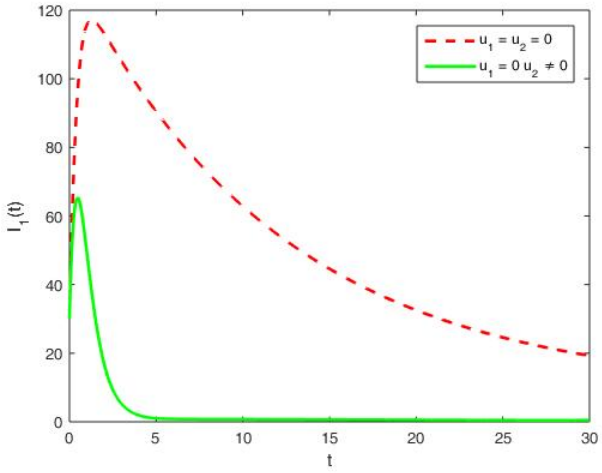

Figure 6: Numerical simulation of TB model showing effect of early treatment on latent class

Table 2: Sensitivity index.

parameter	$\Upsilon^{R_0}_{parameter}$
β	1
Λ	1
γ_1	$\frac{-\gamma_1}{(\alpha_1+\alpha_2+\gamma_1+\mu)}$
γ_2	$\frac{-\gamma_2\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]}{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)](\theta+\delta_1+\gamma_2+\mu)+\alpha_2(\theta+\delta_1+\gamma_2+\mu)^2}$
γ_3	$\frac{-\gamma_3[\alpha_1\theta+\alpha_2(\theta+\delta_1+\gamma_2+\mu)]}{\{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]+\alpha_2(\theta+\delta_1+\gamma_2+\mu)\}(\gamma_3+\delta_2+\mu)}$
δ_1	$\frac{-\delta_1\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]}{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)](\theta+\delta_1+\gamma_2+\mu)+\alpha_2(\theta+\delta_1+\gamma_2+\mu)^2}$
δ_2	$\frac{-\delta_2[\alpha_1\theta+\alpha_2(\theta+\delta_1+\gamma_2+\mu)]}{\{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]+\alpha_2(\theta+\delta_1+\gamma_2+\mu)\}(\gamma_3+\delta_2+\mu)}$
ρ	$\frac{\alpha_1\rho(\gamma_3+\delta_2+\mu)}{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]+\alpha_2(\theta+\delta_1+\gamma_2+\mu)}$
θ	$\frac{\alpha_1\theta[(\delta_1+\alpha_2+\mu)-\rho(\gamma_3+\delta_2+\mu)]}{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)](\theta+\delta_1+\gamma_2+\mu)+\alpha_2(\theta+\delta_1+\gamma_2+\mu)^2}$
α_1	$\frac{\alpha_1[\theta(\gamma_1+\mu)+\rho(\gamma_3+\delta_2+\mu)(\alpha_2+\gamma_1+\mu)-\alpha_2(\gamma_2+\mu)]}{\{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]+\alpha_2(\theta+\delta_1+\gamma_2+\mu)\}(\alpha_1+\alpha_2+\gamma_1+\mu)}$
α_2	$\frac{\alpha_2[\alpha_1(\delta_1+\gamma_2+\mu)+(\gamma_1+\mu)(\theta+\delta_1+\gamma_2+\mu)-\alpha_1\rho(\gamma_3+\delta_2+\mu)]}{\{\alpha_1[\theta+\rho(\gamma_3+\delta_2+\mu)]+\alpha_2(\theta+\delta_1+\gamma_2+\mu)\}(\alpha_1+\alpha_2+\gamma_1+\mu)}$

forward sensitivity index is defined as follows:

$$\Upsilon^X_p = \frac{\partial X}{\partial p} \times \frac{p}{X}.$$

The sensitivity index is presented in Table 2 using the formula defined above. The parameters Λ, β, ρ are directly proportional to the basic reproduction number while the parameters $\gamma_1, \gamma_2, \gamma_3, \delta_1, \delta_2$ are inversely proportional to the basic repro-

Table 3: Sensitivity index value

parameter	$\Upsilon^{R_0}_{parameter}$
β	1
Λ	1
γ_1	−0.7825
γ_2	−0.9786
γ_3	−0.1036
δ_1	−0.0170
δ_2	−0.2738
ρ	0.1071
θ	−0.0351
α_1	0.8333
α_2	0.0446

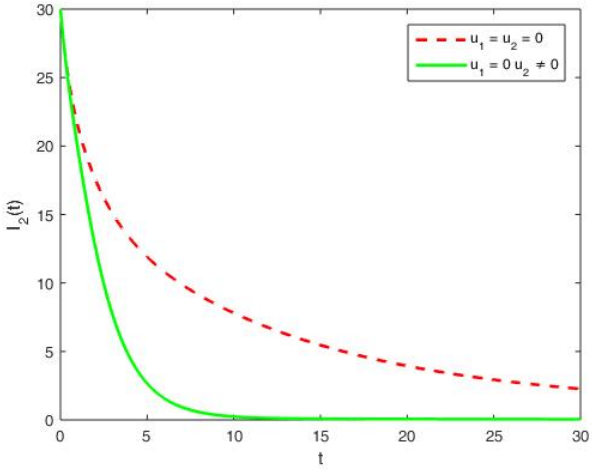

Figure 7: Numerical simulation of TB model showing effect of early treatment on Active class

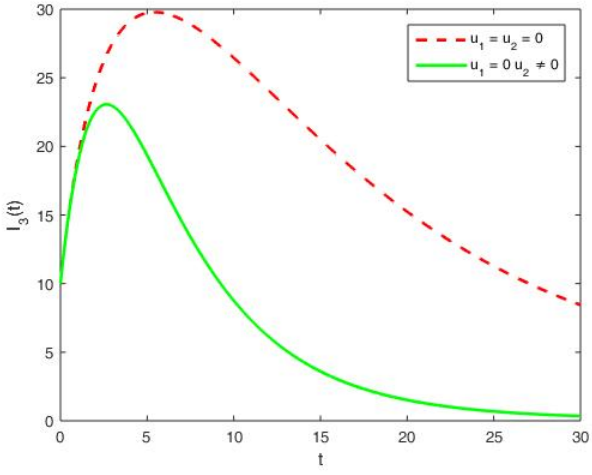

Figure 8: Numerical simulation of TB model showing effect of early treatment on Drug resistant class

duction number. The parameters $\theta, \alpha_1, \alpha_2$ can be both directly or inversely proportional to the basic reproduction number depending on the values of the other parameters associated with them.

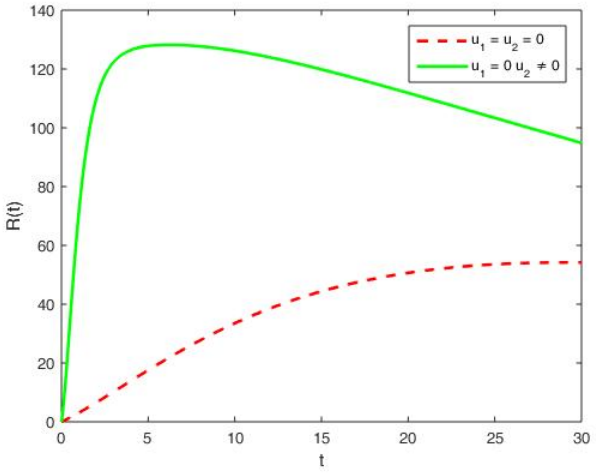

Figure 9: Numerical simulation of TB model showing effect of early treatment on Recovered class

$\Upsilon^{R_0}_{\beta} = 1$ shows that a 1% increase in the transmission rate increases the basic reproduction number by 1% while $\Upsilon^{R_0}_{\beta} = -0.7825$ implies that increasing the effective treatment rate from latent stage by 10% decreases the basic reproduction number by approximately 7.8% as shown in Table 3.

The values of the sensitivity index in Table 2 is presented in Table 3 using parameter values in Table 1.

3.7. Optimal Control

Optimal control analysis is carried out by introducing two control functions $u_1(t)$ and $u_2(t)$ which serves as control into system (1)-(5). The aim of the first control is a preventive control to reduce the spread of tuberculosis among the susceptible and the infectious classes while the second control is the effort to ensure early detection and treatment at the latent stage. The model (1)-(5) becomes

$$\frac{dS}{dt} = \Lambda - \beta(1-u_1)S(\rho I_2 + I_3) - \mu S. \quad (12)$$

$$\frac{dI_1}{dt} = \beta(1-u_1)S(\rho I_2 + I_3) - (\alpha_1 + \alpha_2 + \gamma_1 + u_2 + \mu)I_1. \quad (13)$$

$$\frac{dI_2}{dt} = \alpha_1 I_1 - (\theta + \delta_1 + \gamma_2 + \mu)I_2. \quad (14)$$

$$\frac{dI_3}{dt} = \alpha_2 I_1 + \theta I_2 - (\gamma_3 + \delta_2 + \mu)I_3. \quad (15)$$

$$\frac{dR}{dt} = (\gamma_1 + u_2)I_1 + \gamma_2 I_2 + \gamma_3 I_3 - \mu R. \quad (16)$$

The required optimization problem which involves obtaining the best strategy at minimum cost that minimizes the population within infection classes. This minimization problem can be solved by execution of controls $u_1(t)$ and $u_2(t)$ within the time horizon [0, T]. The objective functional is described as

$$J(u_1, u_2) = \int_0^T (lI_1 + mI_2 + nI_3 + n_1u_1^2 + n_2u_2^2)dt, \quad (17)$$

where T denotes the final time and parameters l, m, n, n_1, n_2 are positive weights to balance the factors.
We consider the state system (12)-(16) with the set of admissible control functions

$$\mathcal{U} = \{u_1, u_2 \in L^1(0,T) \mid 0 \le u_1(t), u_2(t) \le 1 \forall t \in [0,T]\}. \quad (18)$$

Thus, an optimal control u_1^*, u_2^* is obtained such that

$$J((u_1^*, u_2^*) = min\{J(u_1, u_2) : (u_1, u_2) \in \mathcal{U}\}. \quad (19)$$

The existence of the optimal control can be obtained using the result of Fleming and Rishel [21]. The necessary condition that an optimal control system must satisfy come from the Pontryagin's Maximum principle [22]. The principle converts (12)-(17) into problem of minimizing pointwise a Hamiltonian $\mathcal{H}$ relative to u_1 and u_2.

Theorem 3.6. *Problems (12)-(19) with initial values $S(0), I_1(0), I_2(0), I_3(0), R(0)$ and final fixed time T admits a unique optimal solution $(S^*(t), I_1^*(t), I_2^*(t), I_3^*(t), R^*(t))$ with an associated optimal pair (u_1^*, u_2^*) on $[0,T]$. There exists also adjoint variables $\lambda_1, \lambda_2, \cdots, \lambda_5$ satisfying $-\frac{\partial \lambda_i}{\partial t} = \frac{\partial \mathcal{H}}{\partial j}$ where $j = S, I_1, I_2, I_3, R$ with tranversality conditions $\lambda_i(T) = 0$.*

Proof: We define our Hamiltonian as follows:

$$\begin{aligned}\mathcal{H} = lI_1 + mI_2 + nI_3 + n_1u_1^2 + n_2u_2^2 + \lambda_1\left[\Lambda - \beta(1-u_1)S(\rho I_2 + I_3) - \mu S\right] \\ + \lambda_2\left[\beta(1-u_1)S(\rho I_2 + I_3) - (\alpha_1 + \alpha_2 + \gamma_1 + u_2 + \mu)I_1\right] \\ + \lambda_3\left[\alpha_1 I_1 - (\theta + \delta_1 + \gamma_2 + \mu)I_2\right] \\ + \lambda_4\left[\alpha_2 I_1 + \theta I_2 - (\gamma_3 + \delta_2 + \mu)I_3\right] + \lambda_5\left[(\gamma_1 + u_2)I_1 + \gamma_2 I_2 + \gamma_3 I_3 - \mu R\right],\end{aligned}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ describes the associated adjoint functions with the respective states. There exists adjoint functions satisfying

$$\begin{aligned}\frac{d\lambda_1}{dt} &= \beta(1-u_1)(\rho I_2 + I_3)(\lambda_1 - \lambda_2) + \lambda_1\mu. \\ \frac{d\lambda_2}{dt} &= -l + (\alpha_1 + \alpha_2 + \gamma_1 + u_2 + \mu)\lambda_2 - \alpha_1\lambda_3 - \alpha_2\lambda_4 \\ &\quad - (\gamma_1 + u_2)\lambda_5. \\ \frac{d\lambda_3}{dt} &= -m + \beta\rho S(1-u_1)(\lambda_1 - \lambda_2) + (\theta + \delta_1 + \gamma_2 + \mu)\lambda_3 \\ &\quad - \theta\lambda_4 - \gamma_2\lambda_5. \\ \frac{d\lambda_4}{dt} &= -n + \beta S(1-u_1)(\lambda_1 - \lambda_2) + (\gamma_3 + \delta_2 + \mu)\lambda_4 - \gamma_3\lambda_5. \\ \frac{d\lambda_5}{dt} &= \mu\lambda_5.\end{aligned}$$

with the terminal conditions

$$\lambda_1(T) = 0, \lambda_2(T) = 0, \lambda_3(T) = 0, \lambda_4(T) = 0, \lambda_5(T) = 0 \quad (20)$$

Evaluating $\frac{\partial \mathcal{H}}{\partial u_1} = 0$ at $u_1 = u_1^*$, $\frac{\partial \mathcal{H}}{\partial u_2} = 0$ at $u_2 = u_2^*$ and applying standard control arguments involving the bounds in $\mathcal{U}$ gives the characterization u_1^*, u_2^* as

$$u_1^* = min\left(u_{1max}, max\left(0, \frac{\beta S(\rho I_2 + I_3)(\lambda_2 - \lambda_1)}{2n_1}\right)\right).$$

$$u_2^* = min\left(u_{2max}, max\left(0, \frac{(\lambda_2 - \lambda_5)I_1}{2n_2}\right)\right).$$

3.8. Numerical Simulation

The numerical simulation of the optimal control analysis is carried out using parameters and values in Table 1 with initial values $S(0) = 100, I_1(0) = 30, I_2(0) = 30, I_3(0) = 10, R(0) = 0$. The objective function is optimized using the TB prevention control and the results are presented in Figures 2-5. It was observed with about 90 % in the effectiveness of the preventive control, there is a high positive impact on the susceptible class with about 20 % fewer people moving into the infected class as seen in Figure 2. Similarly there is a positive impact in the latent class, with about 50 % reduction at the peak of the class before the end of the intervention as seen in Figure 3. Much impact is not seen in the active class as seen in Figure 4 but a little impact is seen in the drug resistant class as shown in Figure 5.

The impact of early treatment control is seen in the latent compared to the uncontrolled case as seen in Figure 6. The outcome is so significant that it reflected positively on the other two infected classes and recovered class, as seen in Figures 7-9. These strategies suggest that early detection and treatment of TB at the latent stage can reduce the latent population by about 50 % at the peak of the infection when compared to the uncontrolled case. The reduction in latent population also decreases rapidly within a shorter period during the intervention period than in the uncontrolled case. A similar result is obtained for the drug resistant population. The impact of the early control also produced about three times recovery size than in the uncontrolled case.

4. Conclusion

In this research, we have developed a five-system first-order nonlinear differential equation model to characterize tuberculosis (TB) dynamics, incorporating three distinct infected classes. We have rigorously analyzed the boundedness and positivity of solutions, thereby enhancing the robustness of our model. Notably, our model improves upon existing frameworks by differentiating between active and drug-resistant individuals, a distinction overlooked in previous studies by Ojo *et al.* [8] and Das *et al.* [10]. The calculation of the basic reproduction number (R_0), crucial for assessing disease transmission potential, was achieved using the next-generation matrix approach. We have established the local asymptotic stability of the disease-free equilibrium for $R_0 < 1$, with instability prevailing for $R_0 > 1$, indicating the existence of an endemic equilibrium in such cases. Furthermore, employing a suitable Lyapunov function, we have demonstrated the global asymptotic stability of the disease-free equilibrium when $R_0 < 1$.

Our investigation extends to the characterization of optimal control measures, particularly focusing on the impact of preventive and early treatment strategies, elucidated through numerical simulations. The results indicate that both preventive measures and early treatment serve as effective approaches in managing TB infection.

In summary:

- The disease-free equilibrium of TB dynamics is both locally and globally asymptotically stable for $R_0 < 1$.

- A unique endemic equilibrium emerges for $R_0 > 1$.
- Parameters directly proportional to R_0, such as recruitment rate and transmission rate, significantly influence disease spread, while those inversely related, such as treatment rate and disease-induced death, mitigate transmission.
- Sensitivity analysis underscores the efficacy of early treatment at both asymptotic and active stages in reducing R_0.
- Multiple optimal control strategies are imperative for curbing TB prevalence effectively.

These findings contribute to a deeper understanding of TB dynamics and provide valuable insights for the development of targeted intervention strategies aimed at disease control and management.

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