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Using Mathematical Modeling to Understand the Effect of Treatment Efficacy of Two-Strain Model of Tuberculosis

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ABSTRACT
This study focuses on the spread of tuberculosis, a contagious disease caused by Mycobacterium tuberculosis, with a special emphasis on the consequences of drug sensitivity and drug-resistant patients. Tuberculosis treatment normally lasts 6-8 months for newly infected persons, but can extend up to 2.5 years for patients with multidrug resistance. Despite the greater effort put in place to eradicate tuberculosis (TB), it has remained a major global health challenge, particularly in low- and middle-income countries This study presents a mathematical model of tuberculosis transmission patterns in both drug-sensitive and drug-resistant cases. We studied seven (7) compartments: susceptible, latently afflicted with DS-TB, latently infected with DR-TB, infectious with DS-TB, infectious with DR-TB, recovered with DS-TB, and recovered with DR-TB, and mathematically simulated natural growth, population interactions, and treatment effects. Disease-free equilibrium (DFE) and endemic equilibrium (EE) were identified. We determined the basic reproduction number $\left(R_0\right)$, which can be used to manage disease transmission dynamics, and thus established the requirements for local and global disease-free equilibrium stability using the Routh-Hurwitz criterion and the Lasalle-Lyapunov function, respectively. The examination of the stability of the disease-free equilibrium revealed that tuberculosis can be eradicated by reducing the rate of recovery of infected individuals with DS-TB and DR-TB, as well as the rate of natural death. The model's numerical analysis shows that tuberculosis will be eradicated in patients with both DS-TB and DR-TB if efforts to reduce DS-TB and DR-TB transmission rates are increased by continued treatment efficacy.

Keywords:
Tuberculosis,
Mycobacterium,
Drug sensitivity,
Drug-resistance,
Two-strain.

INTRODUCTION

Tuberculosis (TB) is largely caused by Mycobacterium tuberculosis, which attacks the lungs and other respiratory organs (Daniel et al, 1994; Jaramillo, 1999). It may, however, harm other organs, including the kidneys, spine, brain, lymphatic system, and central nervous system (Blower et al, 1996; Murphy et al 2002; Saif et al 2019). An active lung tuberculosis infection is distinguished by a persistent cough with intermittent blood or sputum production, exhaustion, weight loss, fever, and night sweats lasting three weeks or more. In 2023, there were 10.8 million tuberculosis cases reported globally, with 1.2 million in children and 9.4 million in adults (WHO., 2022). In 2023, 55% of tuberculosis cases were males, 33% were females, and 12% were children and young adolescents. The global number of tuberculosis deaths fell in 2023, continuing a trend that began in 2022 following two surges during the worst years of the COVID-19 epidemic (2020 and 2021) (WHO., 2022).
In 2023, 10.8 million tuberculosis cases were reported worldwide, with 1.2 million in children and 9.4 million in adults (WHO., 2022). In 2023, 55% of tuberculosis cases were among men, 33% among women, and 12% among children and young adolescents. The global number of tuberculosis deaths fell in 2023, continuing a trend that began in 2022, following two spikes during the worst years of the COVID-19 pandemic (2020 and 2021) (WHO., 2022).
Despite this progress, tuberculosis is expected to return as the leading cause of death from a single infectious agent (replacing COVID-19). Globally, 8.2 million people were newly diagnosed with tuberculosis in 2023,

up from 7.5 million in 2022 and 7.1 million in 2019, above projections of 5.8 million in 2020 and 6.4 million in 2021 (WHO., 2022). Those newly diagnosed in 2022 and 2023 are likely to include a sizable backlog of patients who contracted tuberculosis in prior years but had their diagnosis and treatment delayed due to COVID-related issues (WHO., 2022). The three most important medical treatments for tuberculosis are vaccines to prevent tuberculosis transmission, active tuberculosis treatment, and preventive medication for people with latent tuberculosis infections to avoid internal reactivation (Graham, et al 2007).

Mathematical modeling is an effective method for assessing the dynamics of tuberculosis (TB) and determining the efficacy of various TB management strategies (Huo et al, 2021; Jaramillo, 1999; Jinhui et al, 2015; Jung et al, 2002; Kim, et al, 2014). Several mathematicians, statisticians, and biologists have created transmission-dynamic tuberculosis (TB) models in recent decades. Blower (1996) developed a theoretical framework for tuberculosis control techniques that evaluates the efficacy of chemoprophylaxis and treatment in eradicating TB epidemics. According to the findings, increased chemoprophylaxis and treatment rates will reduce the severity of tuberculosis epidemics and the likelihood of a latently infected person becoming actively ill. This study discovered that lowering treatment failure rates in disadvantaged countries relative to developed ones is critical for managing tuberculosis epidemics Jinhui et al (2015).

In 2010, Huo et al (2021) created a two-strain transmission dynamic model that includes susceptible, exposed, and infected compartments, each with drug-sensitive and drug-resistant tuberculosis. The global stability of disease-free and mono-existing equilibrium states was determined using dynamic system analysis. According to the findings, if both basic reproduction numbers are less than one, drug-sensitive and drug-resistant tuberculosis would eventually go extinct; otherwise, an epidemic will emerge (Huo et al, 2021).

The majority of real-world issues we face, particularly in the physical, social, and life sciences, may be described using differential equations (Sagir et al, 2023; Abdullahi et al. 2022).

In this paper, we conduct a thorough mathematical and numerical assessment of the features and solutions to our novel two-strain TB model, accounting for both biological and mathematical aspects. We employ the next-generation matrix approach to create analytic formulas for a particular person's basic reproduction numbers of the DS and DR TB strains. This method efficiently generates a table describing the number of new infections induced by each person infected with a specific strain. We understand that these are critical parameters that affect the model's dynamics. We also talk about mono- and co-infection, as well as the criteria for being infection-free.

MATERIALS AND METHODS

Model Formulation

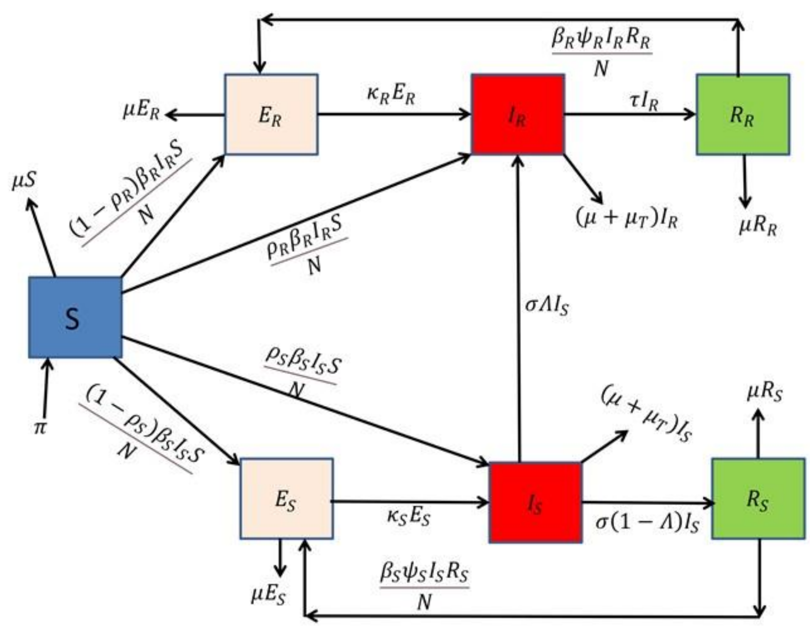

Figure 1: Schematic diagram of the model

Model equations with drug sensitivity and drug resistance and reinfection

$$
\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \left(\frac{\beta_S I_S}{N} + \frac{\beta_R I_R}{N} + \mu\right)S \\
\frac{dE_S}{dt} &= \frac{(1-\rho_S)\beta_S I_S S}{N} + \frac{\beta_S \psi_S I_S R_S}{N} - (\kappa_S + \mu)E_S \\
\frac{dE_R}{dt} &= \frac{(1-\rho_R)\beta_R I_R S}{N} + \frac{\beta_R \psi_R I_R R_R}{N} - (\kappa_R + \mu)E_R \\
\frac{dI_S}{dt} &= \frac{\rho_S \beta_S I_S S}{N} + \kappa_S E_S - (\mu + \mu_T + \sigma)I_S \\
\frac{dI_R}{dt} &= \frac{\rho_R \beta_R I_R S}{N} + \kappa_R E_R - (\mu + \mu_T + \tau)I_R \\
\frac{dR_S}{dt} &= \sigma(1-\Lambda)I_S - \left(\frac{\beta_S \psi_S I_S}{N} + \mu\right)R_S \\
\frac{dR_R}{dt} &= \tau I_R - \left(\frac{\beta_R \psi_R I_R}{N} + \mu\right)R_R
\end{aligned}\right\} \tag{1}
$$

where

$S(0)=S_0, E_S(0)=E_{S_0}, E_R(0)=E_{R_0}, I_S(0)=I_{S_0}, I_R(0)=I_{R_0}, R_R(0)=R_{R_0}, R_R(0)=R_{R_0}$.

Note that $N = S + E_S + E_R + I_S + I_R + R_S + R_R$.

Disease free equilibrium state

The TB-free equilibrium in Model (1) is:

$$E_\Delta = \left(S, E_S, E_R, I_S, I_R, R_S, R_R\right) = \left(\frac{\pi}{\mu}, 0,0,0,0,0,0\right)$$

Endemic equilibrium state

The endemic equilibrium is obtained as:

$$S^* = \frac{\pi}{(\lambda_S+\lambda_R+\mu)}, E_S^* = \frac{A_1 A_2 I_S - \rho_S \lambda_S \pi}{A_1 \kappa_S}, E_R^* = \frac{A_1 A_3 I_R - A_1 \sigma \Lambda I_S - \rho_R \lambda_R \pi}{A_1 \kappa_R}, I_S^* = I_S^*, I_R^* = I_R^*, R_S^* = \frac{\sigma(1-\Lambda)I_S}{(\psi_S \lambda_S + \mu)}, R_R^* = \frac{\tau I_R}{(\psi_R \lambda_R + \mu)} \tag{2}$$

Where:

$$A_1 = \lambda_S + \lambda_R + \mu, A_2 = \mu + \mu_T + \sigma, A_3 = \mu + \mu_T + \tau$$

Reproduction number for both drug sensitivity and drug resistance

The reproduction number is given by:

$$R_{\Delta S} = \rho(FV^{-1}) = \frac{(1-\rho_S)\beta_S \kappa_S + (\kappa_S + \mu)\rho_S \beta_S}{(\kappa_S + \mu)(\mu + \mu_T + \sigma)} \tag{4}$$

and

$$R_{\Delta R} = \rho(FV^{-1}) = \frac{(1-\rho_R)\beta_R \kappa_R + (\kappa_R + \mu)\rho_R \beta_R}{(\kappa_R + \mu)(\mu + \mu_T + \tau)} \tag{5}$$

Local stability of the disease-free equilibrium point with both drug sensitivity and drug resistance

Theorem 5:

The disease-free equilibrium point, E_Δ is locally asymptotically stable if $R_\Delta < 1$ and unstable if $R_\Delta > 1$.

$$J(E_\Delta) = \begin{bmatrix} -\mu & 0 & 0 & -\beta_S & -\beta_R & 0 & 0 \\ 0 & -a_1 & 0 & a_3 & 0 & 0 & 0 \\ 0 & 0 & -a_2 & 0 & a_6 & 0 & 0 \\ 0 & \kappa_S & 0 & -a_4 & 0 & 0 & 0 \\ 0 & 0 & \kappa_R & \sigma\Lambda & -a_7 & 0 & 0 \\ 0 & 0 & 0 & a_5 & 0 & -\mu & 0 \\ 0 & 0 & 0 & 0 & \tau & 0 & -\mu \end{bmatrix} \tag{6}$$

Where:

$$a_1 = (\kappa_S + \mu), a_2 = (\kappa_R + \mu), a_3 = (1-\rho_S)\beta_S,$$
$$a_5 = \sigma(1-\Lambda) \; a_4 = (\mu + \mu_T + \sigma),$$
$$a_6 = (1-\rho_R)\beta_R, a_7 = (\mu + \mu_T + \tau)$$

Given

$$\left|J(E_\Delta) - \lambda I\right| = 0 \tag{7}$$

Substituting equation (6) into equation (7) we obtain

$$\begin{vmatrix} -\mu-\lambda & 0 & 0 & -\beta_S & -\beta_R & 0 & 0 \\ 0 & -a_1-\lambda & 0 & a_3 & 0 & 0 & 0 \\ 0 & 0 & -a_2-\lambda & 0 & a_6 & 0 & 0 \\ 0 & \kappa_S & 0 & -a_4-\lambda & 0 & 0 & 0 \\ 0 & 0 & \kappa_R & \sigma\Lambda & -a_7-\lambda & 0 & 0 \\ 0 & 0 & 0 & a_5 & 0 & -\mu-\lambda & 0 \\ 0 & 0 & 0 & 0 & \tau & 0 & -\mu-\lambda \end{vmatrix} = 0 \qquad (8)$$

From equation (17), we observed that $\lambda_1 = \lambda_2 = \lambda_3 = -\mu$, thus equation (8) reduces to

$$\begin{vmatrix} -a_1-\lambda & 0 & a_3 & 0 \\ 0 & -a_2-\lambda & 0 & a_6 \\ \kappa_S & 0 & -a_4-\lambda & 0 \\ 0 & \kappa_R & \sigma\Lambda & -a_7-\lambda \end{vmatrix} = 0 \qquad (9)$$

Therefore, solving the determinant of equation (9) yields the characteristics equation

$$\lambda^4 + \left(a_1+a_2+a_4+a_7\right)\lambda^3 + \left(a_1a_2+a_1a_4+a_1a_7+a_2a_4+a_2a_7+a_4a_7-\left(a_3\kappa_S+a_6\kappa_R\right)\right)\lambda^2 +$$
$$\left(a_1a_2a_4+a_1a_2a_7+a_1a_4a_7+a_2a_4a_7-\left(a_1a_6\kappa_R+a_3a_7\kappa_R+a_2a_7\kappa_S+a_2a_3\kappa_S\right)\right)\lambda +$$
$$a_1a_2a_4a_7+a_3a_6\kappa_S\kappa_R-(a_1a_4a_6\kappa_R+a_2a_3a_7\kappa_S)=0 \qquad (10)$$

Thus, equation (10) reduces to

$$b_4\lambda^4+b_3\lambda^3+b_2\lambda^2+b_1\lambda+b_0=0 \qquad (11)$$

Where:

$$b_4=1$$
$$b_3=\left(a_1+a_2+a_4+a_7\right)$$
$$b_2=\left(a_1a_2+a_1a_4+a_1a_7+a_2a_4+a_2a_7+a_4a_7-\left(a_3\kappa_S+a_6\kappa_R\right)\right)$$
$$b_1=\left(a_1a_2a_4+a_1a_2a_7+a_1a_4a_7+a_2a_4a_7-\left(a_1a_6\kappa_R+a_3a_7\kappa_R+a_2a_7\kappa_S+a_2a_3\kappa_S\right)\right)$$
$$b_0=a_1a_2a_4a_7+a_3a_6\kappa_S\kappa_R-(a_1a_4a_6\kappa_R+a_2a_3a_7\kappa_S)$$

We apply Routh-Hurwitz criterion which states that all roots of the polynomial (11) have negative real part iff the coefficients b_i, are positive and the determinant of the matrices $H_i>0$ for $i=0,1,2,3,4.$ thus,

$$H_1=b_3=a_1+a_2+a_4+a_7>0$$
$$H_2=\begin{vmatrix} b_3 & b_1 \\ 1 & b_2 \end{vmatrix}=b_3b_2-b_1>0, \text{ iff } b_3b_2>b_1$$
$$H_3=\begin{vmatrix} b_3 & b_1 & 0 \\ 1 & b_2 & b_0 \\ 0 & b_3 & b_1 \end{vmatrix}=b_3\begin{vmatrix} b_2 & b_0 \\ b_3 & b_1 \end{vmatrix}-b_1\begin{vmatrix} 1 & b_0 \\ 0 & b_1 \end{vmatrix}=b_3(\mathrm{b}_1b_2-b_0b_3)-b_1^2$$
$$=b_1b_2b_3-b_0b_3^2-b_1^2=b_1b_2b_3-(\mathrm{b}_0b_3^2+b_1^2)>0 \text{ iff } b_1b_2b_3>b_0b_3^2+b_1^2$$

$$H_4=\begin{vmatrix} b_3 & b_1 & 0 & 0\\ 1 & b_2 & b_0 & 0\\ 0 & b_3 & b_1 & 0\\ 0 & 1 & b_2 & b_0\end{vmatrix}=b_3\begin{vmatrix} b_2 & b_0 & 0\\ b_3 & b_1 & 0\\ 1 & b_2 & b_0\end{vmatrix}-b_1\begin{vmatrix} 1 & b_0 & 0\\ 0 & b_1 & 0\\ 0 & b_2 & b_0\end{vmatrix}$$

$$=b_3\left\{b_2\begin{vmatrix} b_1 & 0\\ b_2 & b_0\end{vmatrix}-b_0\begin{vmatrix} b_3 & 0\\ 1 & b_0\end{vmatrix}\right\}-b_1\left\{1\begin{vmatrix} b_1 & 0\\ b_2 & b_0\end{vmatrix}-b_0\begin{vmatrix} 0 & 0\\ 0 & b_0\end{vmatrix}\right\}$$

$$b_3\left[b_0b_1b_2-b_0^{\,2}b_3)\right]-b_1\left[b_0b_1\right]$$

$$b_0b_1b_2b_3-(\mathrm{b}_0\,b_1^{\,2}+b_0^{\,2}b_3^{\,2})>0 \text{ iff } b_0b_1b_2b_3>(\mathrm{b}_0\,b_1^{\,2}+b_0^{\,2}b_3^{\,2})$$

Therefore, all the eigen values of the polynomial (11) have negative real parts, implying that $\lambda_5<0,\lambda_6<0$ and $\lambda_7<0.$ Since all the values of $\lambda_i<0,$ for $i=1,2,3,4,5,6,7,8.$ when $R_\Delta<1,$ we conclude that the disease-free equilibrium point is locally asymptotically stable.

Global stability of the disease-free equilibrium point with both drug sensitivity and drug resistance

From equation (1)

$$V=\kappa_S E_S+(\kappa_S+\mu)I_S+\kappa_R E_R+(\kappa_R+\mu)I_R$$

$$\dot{V}=\kappa_S\,\dot{E}_S+(\kappa_S+\mu)\,\dot{I}_S+\kappa_R\,\dot{E}_R+(\kappa_R+\mu)\,\dot{I}_R \tag{12}$$

$$=\kappa_S\left(\frac{(1-\rho_S)\beta_S I_S S}{N}+\frac{\beta_S\psi_S I_S R_S}{N}-(\kappa_S+\mu)E_S\right)+(\kappa_S+\mu)\left(\frac{\rho_S\beta_S I_S S}{N}+\kappa_S E_S-(\mu+\mu_T+\sigma)I_S\right)+$$

$$\kappa_R\left(\frac{(1-\rho_R)\beta_R I_R S}{N}+\frac{\beta_R\psi_R I_R R_R}{N}-(\kappa_R+\mu)E_R\right)+(\kappa_R+\mu)\frac{\rho_R\beta_R I_R S}{N}+\kappa_R E_R+\sigma\Lambda I_S-(\mu+\mu_T+\tau)I_R$$

$$=\kappa_S(1-\rho_S)\beta_S I_S+\kappa_S\frac{\beta_S\psi_S I_S R_S}{N}+(\kappa_S+\mu)\rho_S\beta_S I_S-(\kappa_S+\mu)(\mu+\mu_T+\sigma)I_S+$$

$$\kappa_R(1-\rho_R)\beta_R I_R+\kappa_R\frac{\beta_R\psi_R I_R R_R}{N}+(\kappa_R+\mu)\rho_R\beta_R I_R+(\kappa_R+\mu)\sigma\Lambda I_S-(\kappa_R+\mu)(\mu+\mu_T+\tau)I_R$$

$$\le\kappa_S(1-\rho_S)\beta_S I_S+(\kappa_S+\mu)\rho_S\beta_S I_S-(\kappa_S+\mu)(\mu+\mu_T+\sigma)I_S+$$

$$\kappa_R(1-\rho_R)\beta_R I_R+(\kappa_R+\mu)\rho_R\beta_R I_R-(\kappa_R+\mu)(\mu+\mu_T+\tau)I_R+\kappa_R\frac{\beta_R\psi_R I_R R_R}{N}+(\kappa_R+\mu)\sigma\Lambda I_S$$

$$\le(\kappa_S+\mu)(\mu+\mu_T+\sigma)\left(\frac{\kappa_S(1-\rho_S)\beta_S+(\kappa_S+\mu)\rho_S\beta_S}{(\kappa_S+\mu)(\mu+\mu_T+\sigma)}-1\right)I_S+(\kappa_R+\mu)(\mu+\mu_T+\tau)\left(\frac{\kappa_R(1-\rho_R)\beta_R+(\kappa_R+\mu)\rho_R\beta_R}{(\kappa_R+\mu)(\mu+\mu_T+\tau)}-1\right)I_R$$

$$\le(\kappa_S+\mu)(\mu+\mu_T+\sigma)\left(R_{\Delta S}-1\right)I_S+(\kappa_R+\mu)(\mu+\mu_T+\tau)\left(R_{\Delta R}-1\right)I_R \tag{13}$$

Thus, from equation (61), $R_\Delta\le 1$ implies that $\dot{V}\le 0.$ By Lasalle's invariance principle, the largest invariant set Ω, contained $\left\{\left(E_S,E_R,I_S,I_R\right)\in\Omega_E,\dot{V}=0\right\}$ is reduced to the disease-free equilibrium E_Δ. This proves the global asymptotic stability of the disease-free equation on Ω_E.

RESULTS AND DISCUSSION

Simulation Results

Table 1: Variables and parameters values used for computational results

Variable/Parameter	Values	Reference
β_S	0.25	Assumed
β_R	0.25	Assumed
π	200	Jung et al (2002)
μ	$\frac{1}{70}$	MdAbdul et al (2022)
μ_T	0.37	MdAbdul et al (2022)
κ_S	0.129	MdAbdul et al (2022)
κ_R	0.129	MdAbdul et al (2022)
ρ_S	0.1	Bhunu et al (2012)
ρ_R	0.1	Bhunu et al (2012)
τ	0.2	Bhunu et al (2012)
σ	0.94	MdAbdul et al (2022)
Λ	0.07	MdAbdul et al (2022)
ψ_S	0.12	Assumed
ψ_R	0.12	Assumed
$S(0)$	3800	Cagri et al (2012)
$E_S(0)$	1800	Cagri et al (2012)
$E_R(0)$	100	Cagri et al (2012)
$I_S(0)$	200	Cagri et al (2012)
$I_R(0)$	50	Cagri et al (2012)
$R_S(0)$	40	Assumed
$R_R(0)$	30	Assumed

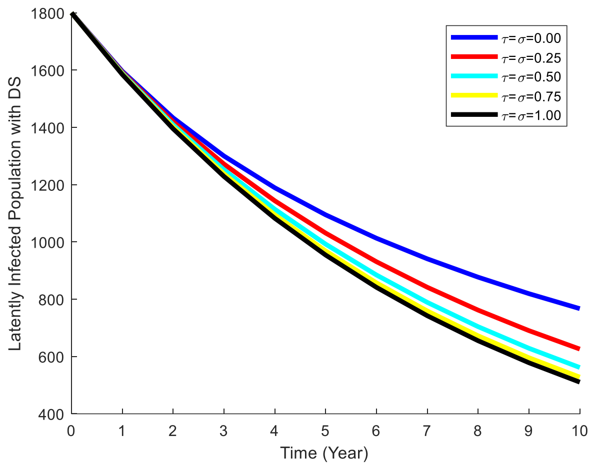

Figure 2: The effect of treatment efficacy of both Drug sensitivity and Drug resistance on latently infected individuals with Drug sensitivity over time. The following parameter values were used: $\tau,\sigma=(0.00-1.00)$, $\beta_S=0.25, \beta_R=0.25$ and $\Lambda=0.07$ All other parameter values were stated in table 1.

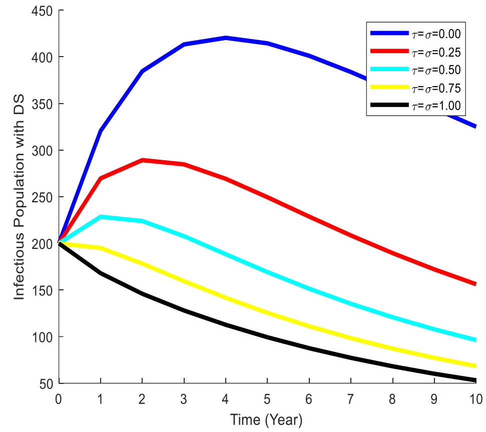

Figure. 4: The effect of treatment efficacy of both Drug sensitivity and Drug resistance on infectious individuals with Drug sensitivity over time. The following parameter values were used: $\tau,\sigma=(0.00-1.00)$, $\beta_S=0.25, \beta_R=0.25$ and $\Lambda=0.07$.All other parameter values were stated in table 1.

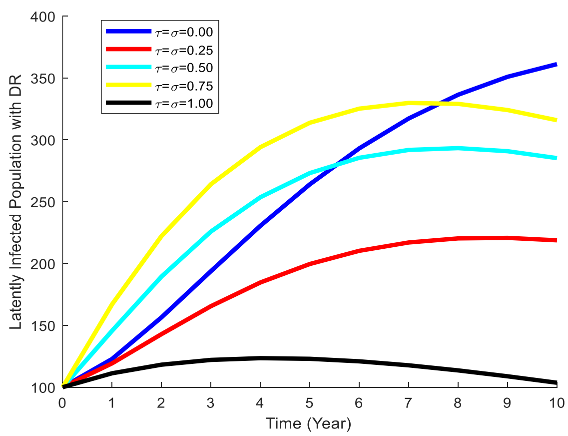

Figure 3: The effect of treatment efficacy of both Drug sensitivity and Drug resistance on latently infected individuals with Drug resistance over time. The following parameter values were used: $\tau,\sigma=(0.00-1.00)$, $\beta_S=0.25, \beta_R=0.25$ and $\Lambda=0.07$ All other parameter values were stated in table 3.

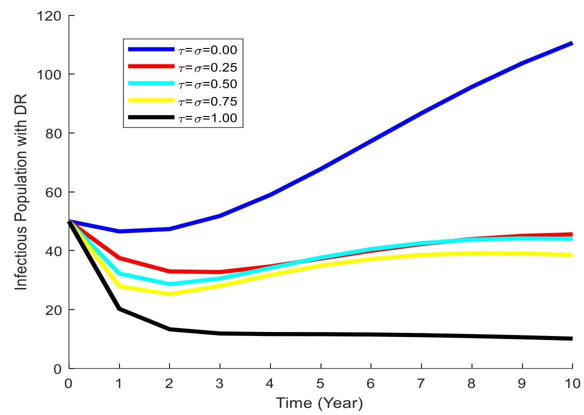

Figure. 5: The effect of treatment efficacy of both Drug sensitivity and Drug resistance on infectious individuals with Drug resistance over time. The following parameter values were used: $\tau,\sigma=(0.00-1.00)$, $\beta_S=0.25, \beta_R=0.25$ and $\Lambda=0.07$. All other parameter values were stated in table 3.

Simulation results for the effect of treatment efficacy of both Drug sensitivity and Drug resistance

Figure (2) shows that there is a significant impact in the latently infected individuals with DS-TB class, implying that as the treatment efficacy of both drug sensitivity and drug resistance rapidly increases, individuals with latently infected with drug sensitivity decrease due to proper treatment. Identifying and treating latently infected individuals with Drug sensitivity becomes more critical in reducing the number of new infections as treatment efficacy for both Drug sensitivity and Drug resistance improves. Figure (3) shows that there is no effect on the latently infected individuals with Drug resistance class.

Figure (4) shows a considerable influence in infectious patients with drug sensitivity classes. This suggests that when the treatment efficacy of both Drug sensitivity and Drug resistance improves, the number of infected individuals with Drug sensitivity drops and stabilizes at a low level due to treatment efficacy, implying that Drug sensitivity is curable. Similarly, Figure (5) follows the same pattern as Figure (11). Therefore, drug resistance is also treatable.

CONCLUSION

In this study, we modified the mathematical model proposed by Sulayman and Abdullah (2023) to account for the dynamics of tuberculosis disease transmission. We investigated the modified model, in which the population is divided into seven compartments: susceptible, latently infected with drug sensitivity, latently infected with drug resistance, infectious with drug sensitivity, infectious with drug resistance, recovered with drug sensitivity, and recovered with drug resistance. The disease-free equilibrium (DFE) and endemic equilibrium (EE) points were identified. The next-generation matrix method was used to determine the reproduction number for both drug sensitivity and drug resistance R_{Δ} . The results showed that the disease-free equilibrium point is locally asymptotically stable when $R_{\Delta} < 1$, indicating that tuberculosis can be eradicated within the population. We found that the disease-free equilibrium point is globally asymptotically stable when $R_{\Delta} \leq 1$, indicating that tuberculosis dies naturally. The model's numerical analysis shows that tuberculosis can be eradicated in patients with both drug sensitivity and drug resistance if efforts are increased to improve ongoing treatment efficacy through the use of the BCG vaccine and other TB drugs.

A basic, but more realistic, deterministic model of TB transmission was provided. In contrast to many tuberculosis models in the literature, we incorporate drug sensitivity classes and drug resistance into the existing model of first-line tuberculosis treatment [9]. An analysis using linearized stability revealed that disease-free equilibrium (DFE) points are locally asymptotically stable (LAS) when $R_0 < 1.$ and globally asymptotically stable (GAS) when $R_0 > 1$.The results of the numerical experiment show that behavioral changes significantly increase the rate at which tuberculosis is eradicated from society.

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