



SENSITIVITY ANALYSIS OF MATHEMATICAL MODELING OF TUBERCULOSIS DYNAMICS WITH A CONTROL MEASURE

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ABSTRACT: *Tuberculosis is a global threat to human existence. A model to investigate the transmission of tuberculosis was constructed and analysed. The threshold quantity (R_0) that predicts the existence or extinction of the disease in a population was computed. It was found that the local stability is asymptotically stable when the basic reproduction number is less than unity at the disease-free – equilibrium point. A Lyapunov function was constructed in order to analyse the global stability which was proved to be globally asymptotically stable when the threshold quantity is less or equal to unity. Sensitivity analysis was conducted on the basic reproduction number in order to determine the parameters of the model that are most sensitive as a way to deduce suitable control measures. Numerical simulations are carried out, discussions were made and results are presented in graphical forms.*

KEYWORDS: Modelling, Tuberculosis TB, Public Campaign, Sensitivity Analysis, Lyapunov Function.



INTRODUCTION

Tuberculosis (TB) is a well-known bacterial infection that predominantly affects the lung of the human. Majorly, TB is initiated by Mycobacterium Tuberculosis Complex (MTBC) [8, 12]. The ailment is a respiratory disease that is contracted by an uninfected person through coughing or sneezing from an infected individual. The germs contacted developed to form tubercles on the lungs of the infected patient and rapidly developed at the primary state, incapacitating smooth breath [9,12, 15 and 16]. The disease affects the lungs, and other internal organs of the patient like the lymph gland, intestine, kidneys, uterus and brain [9]. The first stage of infection is the latent stage before the infected person proceeds to other stages.

Globally, the growth of TB was identified to be 1.1% per capita growth rate and 2.4% as the number of cases per year [6, 14]. It was recorded that about 10 million new TB cases were observed globally in 2017, where India emerged with 2.8 million as the world's largest cases. The fact that there was a decline in the mortality rate from 56/100000/year in 2000 to 32/100000/year but the cases of death recorded was about 1.7 million in 2016 in India as the highest still [13].

TB has been described as one of the diseases leading to death, and Nigeria as a nation is among the countries leading in TB and TB/HIV co-infection [2]. It was further shown that 8% of global cases of TB are found in Africa first approximately 2 billion cases. It was estimated that in every 100,000 people in Nigeria, 219 were infected with the disease yearly, and the most prevalent is the dual-infection TB/HIV with 19.1%, and this causes the death of 115,000 people per year and 39,000 deaths from co-infection. To combat with the spread of TB, the Nigerian government initiated a programme known as the 'National Tuberculosis and Leprosy control programme' located in Abuja in 2016 and an adaptation of the dots strategy for the control of TB in Nigeria [11]. The programme was aimed at eliminating TB cases completely in Nigeria.

TB has been rated as one of the ten diseases responsible for death in the world, although there is no permanent cure for the disease. The symptoms are shown in an individual through cough, chest pain, difficulties in breathing, loss of appetite, loss of weight, fever, cold, and fatigue [9]. A lot of effort has been made to reduce or eradicate TB, and its prevention/treatment is majorly through the use of vaccines such as BCG (Bacille Calmette – Guerin) and the application of Drugs for Tuberculosis (OAT) [12]. Medication for TB is needed for six months duration and is conducted in two phases; inpatient and outpatient [9].

LITERATURE REVIEW

There have been several studies conducted on TB to investigate the transmission of the spread of TB in a given population with different approaches [4,7,9 and 13]. For instance, [9] studied the Time delay of the Tuberculosis Epidemic with Recovery.

Haso et al. [8] studied the tuberculosis transmission model using the compartment SEIRS to analyse the transmission of TB in their own city. The stability analysis adopted the Routh-Hurwitz criterion and proved that the DFEP was stable and the EEP was not. The basic reproduction number R_0 was computed, which depends on seven parameters and was found to be less than one (0.4964). Using real data collected from Chiro, they show that TB cannot spread and eventually die out in the community. In order to control the spread and certainly



eliminate the disease, they stated that the rate of transmission must be kept below 0.4732, and $R_0 < 1$ from their sensitivity analysis.

Nkamba et al. [14] discussed a deterministic epidemic system known as SVELI to investigate the influence of vaccination on TB transmission in Cameroon. They computed the disease-free equilibrium points (DFE) and endemic equilibrium points (EEP) and analysed the stabilities around these points. They show that the basic reproduction number $R_0 > 1$ for is a global asymptotical stability at the endemic equilibrium points, and $R_0 < 1$ for disease-free equilibrium points exist. They stated that the possibility of eliminating TB from the population is certain. Data obtained from literature on Cameroon were used for their simulation. Their result indicated that vaccination alone is insufficient to control TB due to poor coverage and contact rate promoting TB transmission.

Andrawus et al. [1] formulated a TB model consisting of six populations, namely Susceptible S; Latent E; Infected I; First line Treatment R_1 ; Second line Treatment R_2 and Recovered R. It was shown that the system is locally asymptotically stable when R_0 less than one at disease free equilibrium is and the same threshold quantity is greater than one at an endemic equilibrium point. They found out that treating an infectious person at first-line treatment can definitely result in a serious decline in the available cases in society's second-line treatment.

Madakiet al [11] presented a mathematical model by incorporating a measure of control adopted by national tuberculosis and leprosy program. The formulated model population was subdivided into four compartments in order to investigate the transmission between those infected and susceptible populations. The threshold quantity was computed employing a next-generation technique. The local stability was computed to study the behaviour of the modelled population. It was shown that the eigenvalues are all negatives hence stability holds. The implication is that the threshold quantity is less than one. Therefore, this shows that the dynamics are locally asymptotically stable and otherwise unstable at the disease-free equilibrium point. The endemic equilibrium points were determined, and data obtained from the general hospital Potiskum, Yobe State were used for the simulation. The result from the numerical simulation shows that it will be impossible to eliminate TB from Nigeria if adopts the strategy of the national tuberculosis and leprosy program.

This study focuses on analysing TB employing the SLITR model. This aims to describe the transmission and provide suggestions as a control measure for disease eradication in Nigeria. In this study, the researchers intend to explore the dynamics of the SLITR model, where S is susceptible, L is latently infected, I – is actively infected, T for treated individuals, and R for recovered individuals, similar to the model in [11]. In this work, we extended [11] by incorporating the treatment class (T), the public enlightenment campaign by the government and replacing the Exposed individuals with latently infected individuals. We further adopted Lyapunov's direct method and Lasalle's method of Invariance Principle to discuss the stability of a positive endemic equilibrium beyond the scope of [11]. In order to predict the most sensitive parameter (s), the sensitivity analysis was conducted in this paper.



METHODOLOGY

The study uses five compartments representing the populations to explain TB transmission dynamics that led to a system of differential equations. These equations were used to obtain the system threshold quantity, and both the disease-free and endemic equilibrium points were obtained. The local stability of the model at the disease-free equilibrium point was discussed using linearisation approaches. A suitable Lyapunov function was considered in the explanation of global stability analysis.

Model Formulation

Model assumption

- We considered all recruitment into the total population as being susceptible.
- We assume that both L and I are tested for TB and taken to treatment centre T at the rate of τ_1 and τ_2 .
- We assume that those undergoing treatment cannot transmit TB
- In this model, we assume that those that recovered are returned to the susceptible class.
- Individuals at $T(t)$ recovered at the rate of ϕ .

Model description

In this study of the TB model, we consider the entire population subdivided into five populations at time t , as follows; $S(t)$ denote susceptible population, $L(t)$ those infected with TB but does not show symptoms and not infectious called latently infected individuals, $I(t)$ represent those that show symptoms, and infectious are actively infected individuals, $T(t)$ treated individuals and $R(t)$ recovered individuals. The compartment $I(t)$ is considered as the only infectious, and new infection occurs with contact between an infectious person and susceptible, with an incidence rate. The susceptible population increases through the influx of birth or immigration presented by a model parameter Λ and individuals that recovers after being treated at the rate with μ as the rate of natural death for all the classes. As an individual becomes infected with TB, a fraction progress directly to the active stage at the rate of θ and other fraction $(1 - \theta)$ to the latent infected class. The rate at which individuals that are latently infected progress to actively infected is γ , the TB-induced death rate is δ and the rate at which latently infected and actively infected individuals progress for treatment are τ_1 and τ_2 respectively.

From the above assumptions and the diagram describing the populations gives the following odes:

$$\frac{dS(t)}{dt} = \Lambda + \rho R(t) - \mu S(t) - \lambda S(t) \quad (1a)$$

$$\frac{dL(t)}{dt} = (1 - \theta)\lambda S(t) - (\mu + \gamma + \tau_1)L(t) \quad (1b)$$

$$\frac{dI(t)}{dt} = \theta\lambda S(t) + \gamma L(t) - (\mu + \delta + \tau_2)I(t) \quad (1c)$$



$$\frac{dT(t)}{dt} = \tau_1 L(t) + \tau_2 I(t) - (\mu + \phi)T(t) \quad (1d)$$

$$\frac{dR(t)}{dt} = \phi T(t) - (\mu + \rho)R(t)$$

where $\lambda = \frac{\beta(1-\psi)I}{N}$ and $N(t) = S(t) + L(t) + I(t) + T(t) + R(t)$

Equation (1) can be conveniently written as follows:

$$\frac{dS(t)}{dt} = \Lambda + \rho R(t) - (\mu + \lambda)S(t) \quad (2a)$$

$$\frac{dL(t)}{dt} = (1 - \theta)\lambda S(t) - k_1 L(t) \quad (1b)$$

$$\frac{dI(t)}{dt} = \theta\lambda S(t) + \gamma L(t) - k_2 I(t) \quad (2c)$$

$$\frac{dT(t)}{dt} = \tau_1 L(t) + \tau_2 I(t) - k_3 T(t) \quad (2d)$$

$$\frac{dR(t)}{dt} = \phi T(t) - k_4 R(t) \quad (2e)$$

where $k_1 = (\mu + \gamma + \tau_1)$, $k_2 = (\mu + \delta + \tau_2)$, $k_3 = (\mu + \phi)$, $k_4 = (\mu + \rho)$

Table 1. The description of TB variables and parameters of model (1)

Variables	Description
S	Susceptible individuals
L	Latently infected individuals
I	Actively infected individuals
T	Treatment compartment of individuals
R	Recovered individuals

Parameters

Λ	Recruitment rate into the susceptible class
ρ	Rate at which recovered individuals become susceptible
μ	Natural death rate associated with each class
θ	Proportion of individual moving from S to I



$1 - \theta$	Proportion of individual moving from S to L
γ	The rate at which latently infected individual become actively infected
τ_1	Movement rate for latently infected individuals for treatment
τ_2	Movement rate for actively infected individuals for treatment
δ	The rate of death due to TB infection
ϕ	Recovery rate of TB individuals due treatment
$1 - \psi$	Fraction of public enlightenment campaign

Basic properties

In order to describe the meaningfulness of system (1), we shall show that all variables are non-negative for time (t). Indeed, for all $t \geq 0$ the solution of model (1) with positive initial data will remain positive.

Positivity and boundedness of solution

Considering the biologically feasible region, since all the state variables are non-negative for the system (1), hence

$$D = \{S, L, I, T, R, R \in R_+^5 : N \leq \frac{\Lambda}{\mu}\}.$$

It is imperative at this point to show that the set D is positively invariant and a global attractor of the model. This implies that we remain in the non-negative region R_+^5 of the phase space that finally enters and remains in D for initialising any phase trajectory anywhere.

Lemma 1 The model (1) the region D is positively invariant.

Proof: By summing up the equations in equation (1), we have

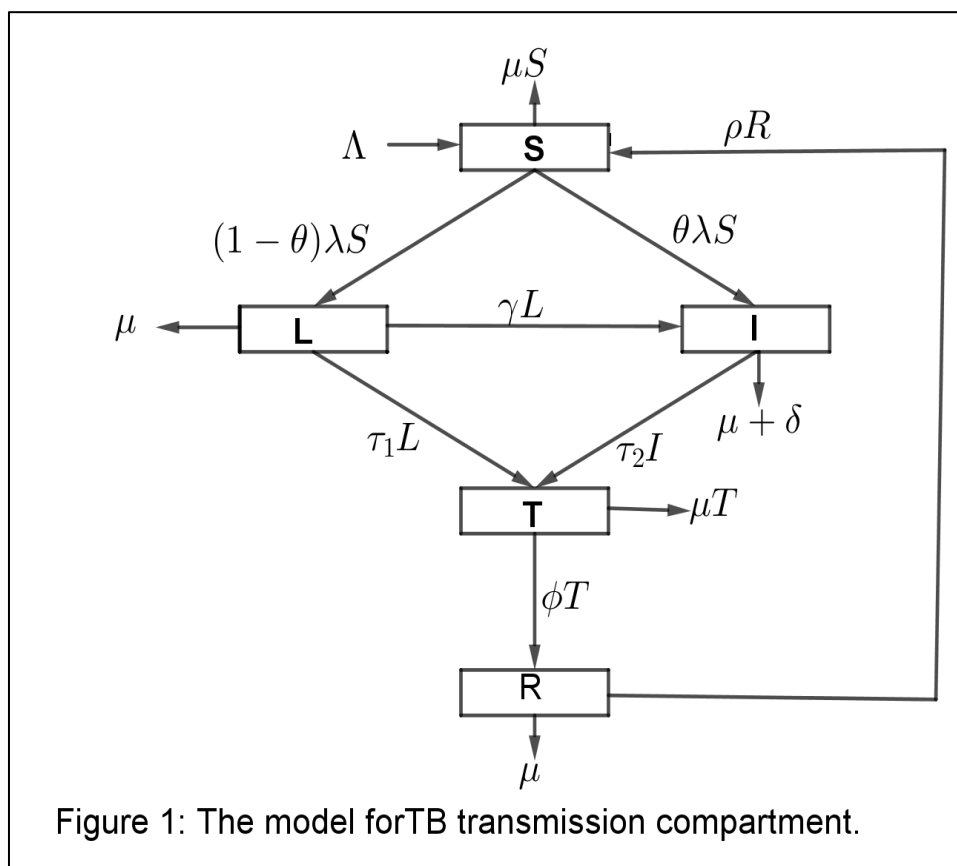
$$\frac{dN}{dt} = \Lambda - \mu N - \delta I \quad (3)$$

At the absence of the disease, δ equals zero, hence equation can be written as

$$\frac{dN}{dt} \leq \Lambda - \mu N \quad (4)$$

Whenever $N > \frac{\Lambda}{\mu}$ implies that $\frac{dN}{dt} < 0$. This can easily be shown from equation (4) that $\frac{dN}{dt}$ is bounded by $\Lambda - \mu N$, from standard comparison theorem, which leads to the solution $N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})$. Indeed, if $N(0) \leq \frac{\Lambda}{\mu}$, it follows that $N(t) \leq \frac{\Lambda}{\mu}$. It can obviously be

shown from this that D is a positively – invariant set described by equation (1). The model can be considered to be mathematically and epidemiologically well-posed with this region [5].



MODEL ANALYSIS

In this section, we present the analysis of TB in equation (2) and compute the existence of both DFE and the endemic equilibrium points.

Asymptotic stability of disease-free equilibrium

The disease-free equilibrium point is a condition where TB does not exist as a disease any longer. The latently infected class and actively infected class are the disease classes in such cases. Therefore, in the absence of disease, then $L^* = I^* = 0$ and solving for S^* in equation (1), gives $S^* = \frac{\Lambda}{\mu}$ and therefore, $DFE = E_0 = (S^*, L^*, I^*, T^*, R^*) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$.

We obtained the basic reproduction number from the linear stability of E_0 using the next generation operator method for the system (1) [7], such that $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius of the next generation matrix. Considering the two matrices F_i and V_i represents the rate of new infection entering the compartment i and the rate of transfer and out of the compartment i in another way respectively. Therefore from the model (1), we have



$$F_i = \left(\frac{\beta(1-\theta)(1-\psi)S(t)I(t)}{N} \quad \frac{\beta\theta(1-\psi)S(t)I(t)}{N} \right) \text{ and } V_i = \left((\mu + \gamma + \tau_1)L(t) \quad (\mu + \delta + \tau_2)I - \gamma L(t) \right)$$

Differentiating F_i and V_i with respect to the state variables, we obtain a 2×2 matrix shown below:

$F = (0 \quad \beta(1-\theta)(1-\psi) \quad 0 \quad \beta\theta(1-\psi))$ and $V = (\mu + \gamma + \tau_1 \quad 0 \quad -\gamma \quad \mu + \delta + \tau_2)$ Then the inverse of V is given as

$$V^{-1} = \begin{pmatrix} 1 & 0 & \gamma & 1 \\ \mu + \gamma + \tau_1 & (\mu + \gamma + \tau_1)(\mu + \delta + \tau_2) & \mu + \delta + \tau_2 & \mu + \delta + \tau_2 \end{pmatrix}$$

It follows that the basic reproduction number is given as

$$R_0 = \rho(FV^{-1}) = \frac{\beta\gamma(1-\psi)(1-\theta) + \beta\theta(1-\psi)k_1}{k_1k_2} \quad (5)$$

where $k_1 = \mu + \gamma + \tau_1$ and $k_2 = \mu + \delta + \tau_2$

Lemma 2 Model (2) is considered to locally asymptotically stable at the DFE if $R_0 < 1$ and not stable if $R_0 > 1$.

The implication of Lemma 3.1 biologically is that by the introduction of few infected individuals into a susceptible would not produce an outbreak except $R_0 > 1$. It is, therefore, imperative to know that in order to control any outbreak of disease; this is essentially predicted by the global asymptotic stability at DFE which will be treated in the next session.

Local stability of disease – free equilibrium, E_0

We shall discuss the local stability of the DFE point $E_0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right)$ by considering the linearised forms of the model (2) at the steady point E_0 . We achieve this by computing the Jacobian matrix given by;

$$J_{E_0} = \begin{pmatrix} -\mu & 0 & 0 & 0 & 0 & 0 & -k_1 & \gamma & \tau_1 & 0 & \beta(1-\psi) & \beta(1-\psi)(1-\theta) & -k_2 + \beta\theta(1-\psi) \\ \tau_2 & 0 & 0 & 0 & 0 & -k_3 & \phi & \rho & 0 & 0 & 0 & -k_4 & \end{pmatrix} \quad (6)$$

The eigenvalues of the Jacobian matrix is computed and evaluated at the DFE, as follows:

$$\begin{vmatrix} -\mu - \lambda & 0 & 0 & 0 & 0 & 0 & -k_1 - \lambda & \gamma & \tau_1 & 0 & \beta(1-\psi) & \beta(1-\psi)(1-\theta) & -k_2 + \beta\theta(1-\psi) - \lambda \\ \tau_2 & 0 & 0 & 0 & 0 & -k_3 - \lambda & \phi & \rho & 0 & 0 & 0 & -k_4 - \lambda & \end{vmatrix} = 0 \quad (7)$$

Using the Jacobian determinant of (7) we obtained the eigenvalues defined by

$\det \det |J_{E_0} - \lambda I| = 0$ where λ are the eigenvalues, it then follow that:

$\lambda_1 = -\mu, \lambda_2 = -k_3$ and the quadratic part gives

$$\lambda^2 + [k_1 - k_2 - \beta\theta(1-\psi)]\lambda + (1 - R_E) = 0$$

Therefore, applying quadratic equation formula,



$$\lambda_4 = \frac{-(k_1 + k_2 - \beta\theta(1 - \psi)) - \sqrt{(k_1 + k_2 - \beta\theta(1 - \psi))^2 - 4(1 - R_E)}}{2}$$

and

$$\lambda_5 = \frac{-(k_1 + k_2 - \beta\theta(1 - \psi)) + \sqrt{(k_1 + k_2 - \beta\theta(1 - \psi))^2 - 4(1 - R_E)}}{2}$$

it is very obvious that $\lambda_4 < 0$ and considering

$$\lambda_5 = \frac{-(k_1 + k_2 - \beta\theta(1 - \psi)) + \sqrt{(k_1 + k_2 - \beta\theta(1 - \psi))^2 - 4(1 - R_E)}}{2} < 0$$

this is possible if $\sqrt{(k_1 + k_2 - \beta\theta(1 - \psi))^2 - 4(1 - R_E)} < k_1 + k_2 - \beta\theta(1 - \psi)$

Simplifying this inequality further to have,

$$1 - R_0 < 0 \Rightarrow R_0 < 1$$

From the Jacobian matrix, it has been shown that all the four eigenvalues are less than zero and the fifth eigenvalue satisfies the condition $R_0 < 1$. Therefore, this shows that the system (1) is locally asymptotically stable as all the eigenvalues are less than one and $R_0 < 1$ is otherwise unstable.

Endemic Equilibrium Point

The persistence of an infection in a given population is usually described by the endemic equilibrium state EEP. Consider $E_1 = (S^*, L^*, I^*, T^*, R^*) > 0$ is the EEP of the model (2). Thus, we rewrite equation (1) as

$$\Lambda + \rho R^* - (\mu + \lambda^*)S^* = 0 \quad (8a)$$

$$(1 - \theta)\lambda^*S^* - k_1L^* = 0 \quad (8b)$$

$$\theta\lambda^*S^* + \gamma L^* - k_2I^* = 0 \quad (8c)$$

$$\tau_1L^* + \tau_2I^* - k_3T^* = 0 \quad (8d)$$

$$\phi T^* - k_4R^* = 0 \quad (8e)$$

where $\lambda^* = \frac{\beta(1-\psi)I^*}{N}$, $k_1 = \mu + \gamma + \tau_1$, $k_2 = \mu + \delta + \tau_2$, $k_3 = \mu + \phi$, $k_4 = \mu + \rho$

Solving for the values of the variables, we have

$$S^* = \frac{\Lambda + \rho R^*}{\mu + \lambda^*} = \frac{\Lambda\alpha\lambda^*}{k_1k_2k_3k_4\mu + \lambda^*\{k_1k_2k_3k_4 - \rho\phi\alpha\}} \quad (9a)$$

$$L^* = \frac{(1-\theta)\lambda^*}{k_1} S^* = \frac{k_2k_3k_4\Lambda(1-\theta)\lambda^*}{k_1k_2k_3k_4\mu + \lambda^*\{k_1k_2k_3k_4 - \rho\phi\alpha\}} \quad (9b)$$



$$I^* = \frac{\lambda^*[\gamma(1-\theta)+\theta k_1]}{k_1 k_2} S^* = \frac{k_3 k_4 \Lambda [\gamma(1-\theta)+\theta k_1] \lambda^*}{k_1 k_2 k_3 k_4 \mu + \lambda^* \{k_1 k_2 k_3 k_4 - \rho \phi \alpha\}} \quad (9c)$$

$$T^* = \frac{[k_2(1-\theta)+\tau_2[\gamma(1-\theta)+\theta k_1]] \lambda^*}{k_1 k_2 k_3} S^* = \frac{k_4 \Lambda \alpha \lambda^*}{k_1 k_2 k_3 k_4 \mu + \lambda^* \{k_1 k_2 k_3 k_4 - \rho \phi \alpha\}} \quad (9d)$$

$$R^* = \frac{\phi [k_2(1-\theta)+\tau_2[\gamma(1-\theta)+\theta k_1]] \lambda^*}{k_1 k_2 k_3 k_4} S^* = \frac{\Lambda \alpha \lambda^*}{k_1 k_2 k_3 k_4 \mu + \lambda^* \{k_1 k_2 k_3 k_4 - \rho \phi \alpha\}} \quad (9e)$$

where $\alpha = \tau_1 k_2(1 - \theta) + \tau_2[\gamma(1 - \theta) + \theta k_1]$.

But $\lambda^* = \frac{\beta(1-\psi)I^*}{N}$

$$\Rightarrow I^* = \frac{N\lambda^*}{\beta(1-\psi)} \quad (10)$$

Equating equation (9c) and (10) to solve for λ^* , we have

$$A\lambda^{*2} + B\lambda^* + C = 0 \quad (11)$$

where

$$A = N[k_1 k_2 k_3 k_4 - \rho \phi \alpha]$$

$$B = k_1 k_2 k_3 k_4 \mu N - k_3 k_4 \Lambda \beta(1 - \psi)[\gamma(1 - \theta) + \theta k_1]$$

$$C = 0$$

For $C = 0$ implies that one of the solutions is $\lambda^*_1 = 0$ corresponding to the DFE point, E_0 . Consider $A\lambda^{*2} + B\lambda^* = 0 \Rightarrow A\lambda^* + B = 0$, obviously, $A\lambda^* + B$ accounts for the existence of the DFE point. As we observed equation (11) it clearly indicated that there is a unique EEP but the focus is on $C = 0$. It then follows that the existence of the unique EEP has two possible conditions, that is $B < 0$ and $B^2 - 4AC = 0$.

Case I: Setting $B < 0$ gives,

$$\{k_1 k_2 k_3 k_4 \mu N - k_3 k_4 \Lambda \beta(1 - \psi)[\gamma(1 - \theta) + \theta k_1]\} < 0$$

$$1 - \frac{\Lambda}{\mu N} \cdot R_0 < 0 \quad \text{But } N(t) \leq \frac{\Lambda}{\mu} \text{ Therefore, } 1 - \frac{\Lambda}{\mu} \times \frac{\mu}{\Lambda} R_0 < 0$$

$$1 - R_0 < 0 \Rightarrow R_0 > 1$$

Case II: $B^2 - 4AC = 0$.

$$\Rightarrow B^2 = 0 \text{ that is, } k_1 k_2 k_3 k_4 \mu N - k_3 k_4 \Lambda \beta(1 - \psi)[\gamma(1 - \theta) + \theta k_1] = 0$$

$$\Rightarrow 1 - R_0 = 0 \text{ so } R_0 = 1$$



Global Stability

We shall construct a Lyapunov function which depends on the infected compartment only to discuss the global stability of DFE of the model (2) and investigate the endemic equilibrium point.

Global stability of the disease-free equilibrium, E_0

Theorem 1 If $R_0 < 1$, the disease-free equilibrium point, E_0 of model system (2) is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: In view of [10] work, we define the Lyapunov function by considering equations (2a) – (2e) on the infected classes where $B_1 > 0$ and $B_2 > 0$, thus

$$V = B_1 L + B_2 I$$

$$\dot{V} = \dot{B}_1 L + \dot{B}_2 I \quad (12)$$

$$\begin{aligned} &= B_1[(1 - \theta)\lambda S - k_1 L] + B_2[\theta\lambda S + \gamma L - k_2 I] \\ &= \lambda S[B_1(1 - \theta) + B_2\theta] - L[B_1 k_1 - B_2\gamma] - I[B_2 k_2] \end{aligned} \quad (13)$$

Equating the coefficient of both λS to the numerator and I to the denominator of equation (5) and L to zero, to have

$$B_1(1 - \theta) + B_2\theta = \gamma(1 - \theta) + \theta k_1 \quad (14)$$

$$B_1 k_1 = B_2 \gamma \quad (15)$$

$$B_2 k_2 = k_1 k_2 \quad (16)$$

Solving equations (14) - (17), we have

$$B_2 = k_1 \text{ and } B_1 = \gamma \quad (17)$$

Substituting equation (17) into (13)

$$\begin{aligned} \dot{V} &= \lambda S[\gamma(1 - \theta) + \theta k_1] - I k_1 k_2 \\ \dot{V} &\leq k_1 k_2 I [R_E - 1] \\ \dot{V} &\leq 0 \text{ if } R_E \leq 1 \end{aligned} \quad (18)$$

$$\text{This indicated that } \dot{V} < 0 \text{ if } R_0 < 1 \quad (19)$$



The inequality is satisfied at $R_0 = 1$ and $L = I = 0$. We draw our conclusion from the LaSalle's invariance principle cited in Theorem 3. 1 below that the DFE is globally asymptotically stable as $S \rightarrow \frac{\Lambda}{\mu}$ for $t \rightarrow \infty$ at $L = I = 0$.

Theorem 2 [10] (La Salle Invariance Principle) Let $H(x)$ be a locally Lipschitz function defined over a domain $G \subset R^n$ and $\Omega \subset G$ be a compact set that is positively invariant concerning $\dot{x} = H(x)$. Let $V(x)$ be a continuously differentiable positive definite function on G such that $\dot{V}(x) \leq 0$ in Ω for all $x \in G$. Let $E = [x \in \Omega | \dot{V}(x) = 0]$, and M be the largest invariant set in E . Then every solution starts in Ω approaches M as $t \rightarrow \infty$.

Sensitivity Analysis of TB model

At this point, we shall conduct the sensitivity analysis of the eight parameters of the above model. This analysis indicates how a parameter h would behave as a result of a small change in parameter values, defined as:

$$S_h = \frac{\partial R_0}{\partial h} \times \frac{h}{R_0} \quad (20)$$

It follows that the sensitivity analysis of this model is

$$S_\beta = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1$$

$$S_\psi = \frac{\partial R_0}{\partial \psi} \times \frac{\psi}{R_0} = -\frac{\psi}{1 - \psi}$$

$$S_\gamma = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = \frac{\gamma(1 - \theta)(\mu + \tau_1)}{(\mu + \gamma + \tau_1)[\gamma + \theta(\mu + \tau_1)]}$$

$$S_\theta = \frac{\partial R_0}{\partial \theta} \times \frac{\theta}{R_0} = \frac{\mu(\mu + \tau_1)}{\gamma + \theta(\mu + \tau_1)}$$

$$S_{\tau_1} = \frac{\partial R_0}{\partial \tau_1} \times \frac{\tau_1}{R_0} = -\frac{\gamma(1 - \theta)}{(\mu + \gamma + \tau_1)[\gamma + \theta(\mu + \tau_1)]}$$

$$S_\delta = \frac{\partial R_0}{\partial \delta} \times \frac{\delta}{R_0} = -\frac{\delta}{\mu + \delta + \tau_2}$$

$$S_{\tau_2} = \frac{\partial R_0}{\partial \tau_2} \times \frac{\tau_2}{R_0} = -\frac{\tau_2}{\mu + \delta + \tau_2}$$

$$S_\mu = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\mu[\mu\theta(\mu + 2\tau_1) + \gamma(2\mu + \gamma) + \tau_1(\theta\gamma +)]}{(\mu + \gamma + \tau_1)(\mu + \delta + \tau_2)[\gamma + \theta(\mu + \tau_1)]}$$

It can be clearly seen that, the contact rate β , positively influences the transmission of tuberculosis disease. Controlling the transmission of TB attention is needed to enhance the reduction of contact rate otherwise, the population ceases to exist. The parameters: ψ , δ , μ , and τ_2 influence the transmission of TB disease negatively which epidemically implies that increasing the values of these parameters, consequently reduces the population of humans



infected with TB disease. Similarly, the same scenario occurs with τ_1 if $\theta < 1$. But in the case of θ , the spread of TB is continuously positive, which means that fast propagation of TB enhances the pandemic. In order to reduce its spread, good ventilation and good hygiene should be encouraged, people should be enlightened to cover their mouths with tissues or their hands when they cough or sneeze. Thereafter wash their hands or throw the tissue used into a waste bin. Visitation should be curtailed either to those that are sick or visiting the sick. Furthermore, the sensitivity of γ is similar to the fast propagation of TB if $\theta < 1$.

Numerical simulation

The data used in the numerical simulation of the model were obtained from the record given during the 2023 Tuberculosis Day celebration in March 24 in Abuja, Nigeria and some from works of literature.

Estimation of Parameters

On Tuberculosis Day, March 24th, 2023 in Nigeria, the Senior Programme officer with KNCV, Dr Cynthia Onwuteaka said, the prevalence rate for TB is 219 for every 100,000 people among the entire population of about 200 million in the country [17]. Therefore, the total number of those infected with tuberculosis will be

$$I = \frac{219}{100,000} \times 2 \times 10^8 = 438,000$$

The death rate μ can be expressed as the inverse of life expectancy at birth and Nigeria's life expectancy for 2023 is given as 55.75 years. Hence, the natural death rate, μ can be estimated to be $\mu = \frac{1}{55.75} = 0.017937$ per year. It is also known that the estimation of the recruitment number Λ can be made from the expression of the feasible region represented by $\Lambda = N \times \mu = 3,587,400$.

According to WHO as cited by [3] about 1.1 million people are being treated with an estimated average of 1.05 million recoveries and about 250 000 people die due TB yearly. It follows that

$$\text{The rate of death by TB } \delta = \frac{\text{number of people infected due to TB}}{\text{total number of infected population}} = \frac{250,000}{438,000} = 0.570776$$

Table 2 shows the estimation of the rest of the variables and parameters in a similar computation as illustrated above.

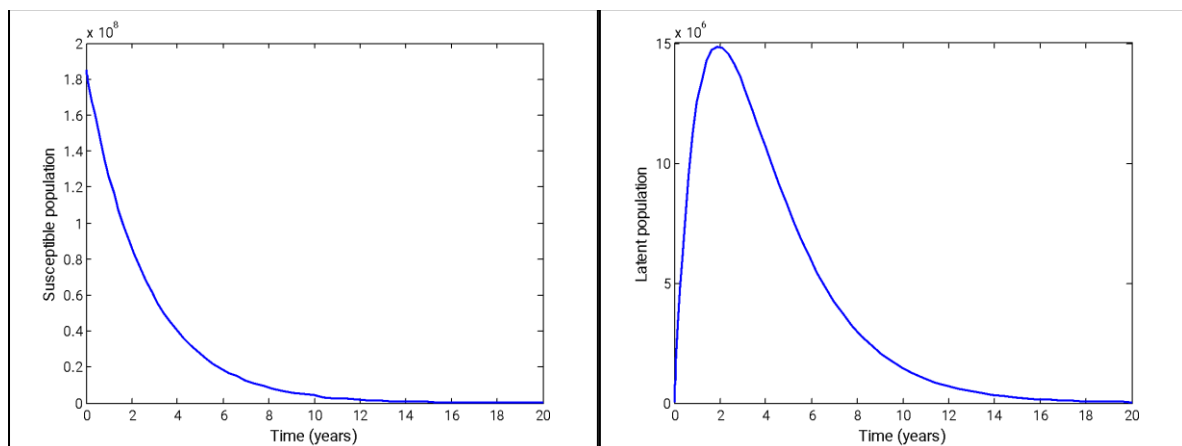
Table 2: Indicate the values for population – independent parameters of TB (yr^{-1})

Variables/Parameters	Values	Source
N	200000000	[17]
S	185000000	[17]
L	185000000	[17]
I	438000	Estimated
T	110000	[16]



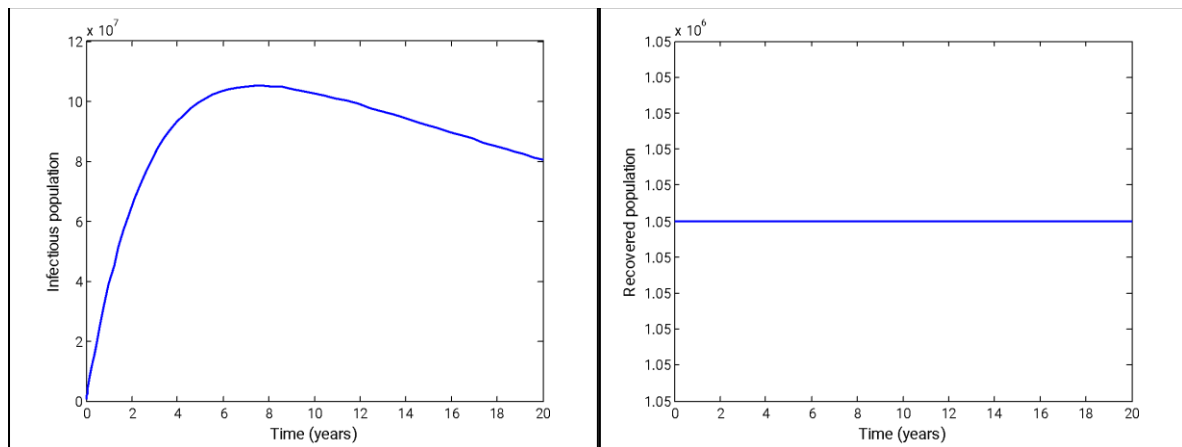
R	105000	[3]
Λ	3587400	Estimated
μ	0.17937	[2]
ϕ	0.009615	Estimated
β	0.398181	[9]
γ	0.1153846	[2]
δ	0.570776	Estimated
λ	0.00035	[4]
τ_1	0.25	[15]
τ_2	0.1	[15]
ρ	0.1	[11]
θ	0.1	[11]
ψ	0.6	[2]

The Plots of population without treatment



(a)

(b)

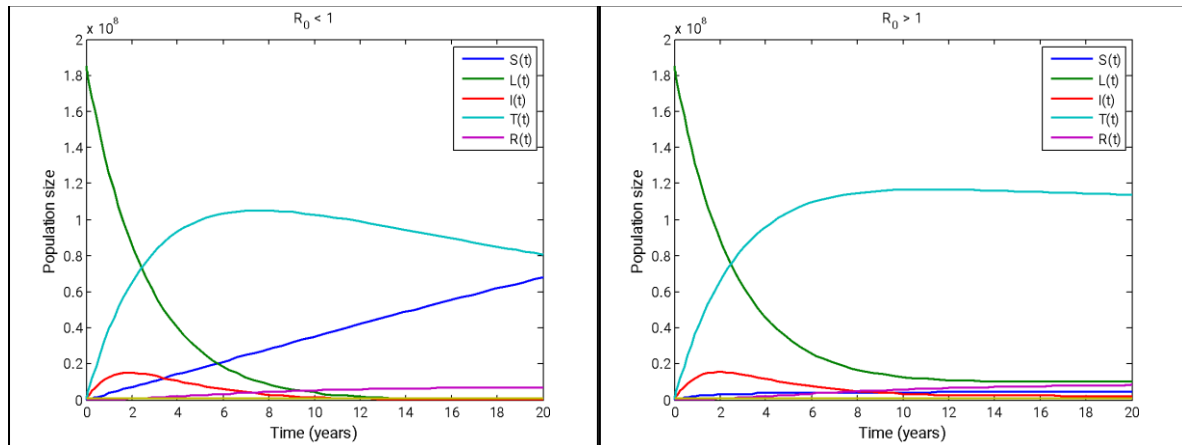


(c)

(d)

Figure1: The plots behaviour of populations without treatment.

The Equilibrium points of the SLITR model

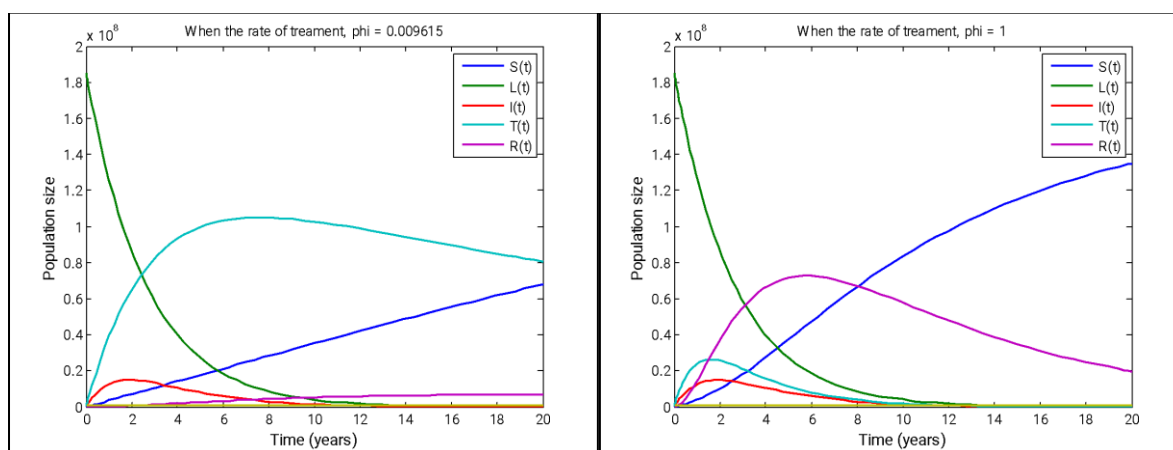


(a)

(b)

Figure 2: The plots show (a) $R_0 < 1$ and (b) $R_0 > 1$ for both $\beta=0.39181$ and 1.0 respectively.

Effects of Treatment on Recovered Individuals



(a)

(b)

Figure 3: Shows the effects of treatment on populations

RESULTS AND DISCUSSION

Figure 1: Illustrate the behaviour of populations without treatment: (a) Susceptible population (b) Latent population (c) Infected population and (d) Recovery population. The parameter values used are found in Table 2. The plots found in Figure 1 demonstrated the behaviour of the model in the absence of treatment. In (a) the susceptible individuals decrease furnishes (b) latent population with more individuals which consequently decreases resulting in the increase in (c) infectious population. The absence of treatment must be responsible for this behaviour. Although, the infectious population does not continue endlessly but natural immunity may cause the infected population to decline. In (d) is a phenomenon where there is no recovery in the absence of treatment.

The two graphs above in Figure 2 illustrate the behaviour of the dynamic when the TB goes to extinction and persists. In 2a, the basic reproduction number is less than one with a contact rate of 0.39181. The graph portrays that the disease can die off from the population with a less contact rate. However figure 2b, shows that the threshold is greater than one when the contact rate is 1. This results in a decrease in the population of susceptible, latent, and recovery classes. This, indeed, confirms the above analytical analysis stated in Section 3 above.

The impacts of treatment are reflected in Fig3. Figure 3a indicated when the rate of those recovered is 0.009615 and when it increases to 1. The implication is that there is a corresponding increase in recovery and susceptible populations and, consequently, a decrease in the population of those treated.



CONCLUSION

The purpose of this paper is to examine the behaviour of the spread of TB in Nigeria and whether it can be eradicated or not. From the computation of R_0 using the next generation methods, the derived basic reproduction number has eight parameters centred on four compartments, namely: Susceptible, latently infected, actively infected and treatment class. It follows from the expression of R_0 , that the most important parameters worth noting that can promote the spread of TB are the contact rate and fast TB propagation rate. This result is confirmed by sensitivity analysis. Indeed, a proper public enlightenment campaign reduces the contact rate and, consequently, the spread of TB as it gives the populace an awareness of the danger of TB disease. The DFE of the model formulated was shown to be locally asymptotically stable if $R_0 < 1$ and the implication is that TB will be eradicated in Nigeria. We also prove the existence and uniqueness of the EEP using Lyapunov function that it globally asymptotically stable for $R_0 > 1$. A Numerical simulation was carried out that agrees with the facts stated about the threshold quantity. It was shown from the simulation that treatment plays a crucial role in reducing the population of those transmitting the disease.

FUTURE RESEARCH

This model has addressed some questions in connection with the spread of TB in Nigeria through the results obtained. However, this work can be expanded further to accommodate some aspects, like the cost analysis. This will enhance the stakeholder insight on the financial implication in order to combat TB in Nigeria.

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