IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

Sensitivity Analysis of Mathematical Modelling of Tuberculosis Disease With Resistance to Drug Treatments

Mufutau,R.A.[1*], Akinpelu,F. [2]

1,2. Department of Mathematics, University of Lagos, Nigeria
*Corresponding author: amufutau@unilag.edu.ng

Article Info
Received: 13 October 2020 Revised: 1 February 2021
Accepted: 7 February 2021 Available online: 16 February 2021

Abstract

Drug resistance to the line of treatment is also of concerns in the control of Tuberculosis disease in the world [11], an individual with drug resistance will still retain the disease even after several treatment. In this study, we consider a mathematical model of a tuberculosis disease with resistance to the first line of treatment, taking into consideration population of children and adults. We considered six different compartment ($S_1S_2EIR_HR$), an extension of SEIR model by introducing two different susceptible classes (S_1S_2) and drug resistance(R_H) to the first line of treatment. The system was described by an ordinary differential equation, which was solved algebraically to obtained the equilibrium point (disease free and endemic equilibrium point). The next generation matrix was employed to evaluate the basic reproduction number and column reduction matrix to get the local stability of the systems. It was observed that the age group had bigger effect on the control of TB. The drug resistance had a little effect on the total control of the disease. At the end, three effective measure were found,that would help reach the major goal of the World Health Organization(WHO)which includes: to reduce the exposed rate of the disease especially in the adults, increase the recovery rate and reduce the transmission rate of the adults.

Keywords and Phrases: Tuberculosis, Resistance to Drug, Basic Reproduction number, Equilibrium, Stability, Sensitivity Analysis.
MSC2010:92B05, 92D30, 93A30

1 Introduction

Tuberculosis (TB) remains a major cause of ill health and is one of the top 10 causes of death worldwide. An estimated 10.0 million people fell ill with TB in 2018, a number that has been relatively stable in recent years. Globally, there were 1.2 million TB deaths among HIV-negative people in 2018 (a 27 percent reduction from 1.7 million in 2000) and an additional 251 000 deaths among HIV-positive people (a 60 percent reduction from 620 000 in 2000) [11].

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

Since 2007, TB has been the leading cause of death from a single infectious agent, ranking above HIV/ AIDS. TB affects people of both sexes in all age groups but the highest burden is in adult men, who accounted for 57 percent of all TB cases in 2018. By comparison, adult women accounted for 32 percent and children for 11 percent. Among all TB cases, 8.6 percent were people living with HIV. Geographically, most TB cases in 2018 based the World Health Organization (WHO)records [11]consist of South-East Asia (44 percent), Africa (24 percent) and the Western Pacific (18 percent), with smaller shares in the Eastern Mediterranean (8 percent), the Americas (3 percent) and Europe (3 percent). Eight countries accounted for two thirds of the global total: India (27 percent), China (9 percent), Indonesia (8 percent), the Philippines (6 percent), Pakistan (6 percent), Nigeria (4 percent), Bangladesh (4 percent) and South Africa (3 percent) [11].

The burden of drug-resistant TB is of major interest and concern at global, regional and country levels. In 2018, there were approximately half a million new cases of rifampicin-resistant TB (of which 78 percent had multidrug-resistant TB). The three countries with the largest share of the global burden were India (27 percent), China (14 percent) and the Russian Federation (9 percent). Globally, 3.4 percent of new TB cases and 18 percent of previously treated cases had MDR/RRTB, with the highest proportions (greater than 50 percent in previously treated cases) in countries of the former Soviet Union [11].

In 2018, The Federal Ministry of Health has declared a year to accelerate finding and notification of TB cases in Nigeria. The huge gap in TB case finding is much higher among children aged zero to 14 with a child proportion of seven per cent for 2017. in order to improve the TB case finding Nigeria has added active case-finding in key affected populations. The health minister said this included people living with HIV, children, urban slum dwellers, prisoners, migrants, internally displaced people and facility based health care workers.Over 11,500 TB cases were detected through active house to house case searching in 2017. Although this is a useful initiative, the number of TB cases detected is a small percentage of the missing 300,000 cases of TB in Nigeria. It estimated by the WHO that 30,000 children get TB in Nigeria each year. There are also 47,000 children that are eligible to receive preventative treatment, that would help to prevent them from getting TB. However, only about 8,500 children actually receive this preventative treatment. Many researchers has work on dynamics of tuberculosis, but few work has be done on the dynamics of tuberculosis disease with resistance to drug.

The first tuberculosis model was developed by Waaler et al [3], they use mathematical model to study the epidemiology of tuberculosis disease. Liu and Yang [1], McCluskey and Van den Driessche [9] both study the mathematical model of tuberculosis with two latent periods and treatment interruptions. Ozcaglar et al [8] observed and predicted epidemiological models which reviews earlier study on modeling different aspects of tuberculosis dynamics. They observed that there is an increase in the tuberculosis in 1990s and the emergence of drug- resistant in the first decade of the 21st century. Ronoh et al [4], Yu et al [5] and Gupta et al [6] considered mathematical model of tuberculosis disease with drug resistance effect an SEIRR model, he failed to consider the age group factor of the population and also the effect of each parameters was not considered (sentivity Analysis). Fofana et al [7] also investigate multistrain mathematical model to investigate the role of pyrazinamide in the emergence of extensively drug-resistant tuberculosis. Greenhalgh et al [12] use a mathematical model to study the impact of awareness programs on an infectious disease outbreak with two susceptible (aware susceptible and unaware susceptible) . Okuonghae and Ikhimwin [2] consider the dynamic of a mathematical model for tuberculosis with variability in susceptibility and disease progression due to difference awareness level.

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

In 2019, Omale et al [13] formulate the mathematical modelling of dynamics of tuberculosis disease and its control, it was showed that vaccination rate decrease the susceptible population . Also in 2020,Omale et al [14] determine the Global stability and sensitivity index of the modelled problem in [13], and it was found that the model Endemic equilibrium point is globally asymptotically stable and the recovery rate of the infected but treated, and the rate at which the vaccinated recovered due to vaccine efficiency decrease the basic reproduction number of the model.

In this paper, we formulate a mathematical model of tuberculosis taking into consideration two susceptible classes (children and adults) and resistance to the first line of treatment.

2 Model Formulation

In this section, we introduce a nonlinear tuberculosis (TB) model with resistance to the first line of treatment. The entire population is classified into five classes: susceptible (S), exposed (E), infectious (I), resistance to drug treatment (R_H) and recovered (R). The susceptible clas s was further divided into two age groups: childhood (S_1) and Adults (S_2). It is assumed that the only way of exit or death is through the natural death μ or death from the tuberculosis disease ϵ. The member of susceptible classes (S_1) and (S_2) move to the exposed class (E) due to infection at the rate of α and β. The member of exposed class moves to infectious class (I) due to lack of treatment or immunity at the rate of σ, while member of infectious class moves either to the recovery class after the first treatment or resist the first line of treatment and moves to drug resistance class (R_H), then after multiple treatment, the drug resistance class (R_H) moves to recovery (R).

2.1 Model Diagram

The figure 1 below represent the transmission of tuberculosis diseases using think arrow to describe the movement of the compartments.

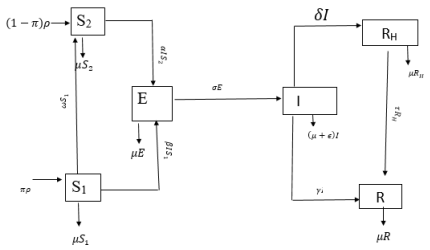

Figure 1: Schematic digram of the model

2.2 System of the Equations

The model for the TB is given by the following deterministic system of non linear differential equation, a flow diagram of the model is depicted in figure 1, and the associated variables and

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

parameters as described in table 1 and 2 respectively.

$$\frac{dS_1}{dt} = \pi\rho - \mu S_1 - \omega S_1 - \beta I S_1 \tag{2.2.1}$$

$$\frac{dS_2}{dt} = (1-\pi)\rho + \omega S_1 - \mu S_2 - \alpha I S_2 \tag{2.2.2}$$

$$\frac{dE}{dt} = \beta I S_1 + \alpha I S_2 - \mu E - \sigma E \tag{2.2.3}$$

$$\frac{dI}{dt} = \sigma E - (\mu + \epsilon) I - \delta I - \gamma I \tag{2.2.4}$$

$$\frac{dR_H}{dt} = \delta I - (\mu + \tau) R_H \tag{2.2.5}$$

$$\frac{dR}{dt} = \gamma I + \tau R_H - \mu R \tag{2.2.6}$$

Table 1: Description of State Variables

varables	Description
$S_1(t)$	Susceptible Child
$S_2(t)$	Susceptible Adult
$E(t)$	Exposed Human
$I(t)$	Infected Human
$R_H(t)$	Resistant to the first line of treatment
$R(t)$	Recovered Human

Table 2: Descriptions of Parameters

Parameters	Description
$\pi\rho$	Recruitment rate from the childhood
$(1-\pi)\rho$	Proportion of the Adult
μ	Natural death rate for the various compartment
β	Transmission rate of tuberculosis from the child
ω	Rate Child from to the Adulthood
α	Transmission rate of tuberculosis from the Adult
σ	Rate of human moving from the exposed class to the infectious class
δ	Rate of human resistance to the first line of treatment
ϵ	Death rate due to the tuberculosis disease
γ	Recovering rate
τ	Recovering rate after several treatment due to the drug resistance

3 Model Analysis

3.1 Existence, Uniqueness and Boundedness of the systems of equations

Theorem 3.1 *for any initial value $p \in \Re^6$, system (1) to (6) has a unique nonnegative solution for all $t \geq 0$*

Proof.

$$N(t) = S_1(t) + S_2(t) + E(t) + I(t) + R_H(t) + R(t), \tag{3.1.1}$$

$$\frac{dN(t)}{dt} = \frac{dS_1(t)}{dt} + \frac{dS_2(t)}{dt} + \frac{dE(t)}{dt} + \frac{d1(t)}{dt} + \frac{dR_H(t)}{dt} + \frac{dR}{dt},$$

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

By adding all the equation, (1)to (6),

$$\frac{dN(t)}{dt} = \rho - \mu N(t) - \tau I \leq \rho - \mu N(t),$$

$$\frac{dN(t)}{dt} \leq \rho - \mu N(t). \tag{3.1.2}$$

It is clear that, if $N(t) \geq \frac{\rho}{\mu}$ and $\frac{dN(t)}{dt} \leq 0$, then the solutions of equation (1) to (6) with non-negative initial value are bounded and exit on the interval $[0, +\infty)$.

3.2 Positivity of the solution

For the model to be epidemiologically meaningful and well posed, we need to prove that the state variables are nonnegative i.e $\forall\, t \geq 0$.

Theorem 3.2 *: Let*

$$\Omega = [(S_1, S_2, E, I, R_H, R) \in \Re^6 : S_1 + S_2 + E + I + R_H + R]$$

then the solution $(S_1(t), S_2(t), E(t), I(t), R_H(t), R(t))$ *of the equation (1)to (6) are positive* $\forall\, t \geq 0$

Proof.

For $(S_1(0) \geq 0, S_2(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R_H(0) \geq 0, R(0) \geq 0)$ then,equation (1)-(6)

$$\frac{dS_1}{dt} \leq \pi\rho - (\mu + \omega)S_1 \tag{3.2.1}$$

by solving, we have

$$S_1(t) \leq \frac{\pi\rho}{\mu + \omega} + c\, e^{-(\mu+\omega)t}. \tag{3.2.2}$$

Applying the initial condition $t \in [0, +\infty)$

$$S_1(t) \leq \frac{\pi\rho}{\mu + \omega} + c, t = 0$$

$$\leq \frac{\pi\rho}{\mu + \omega}, \quad t \to \infty,$$

$$0 \leq S_1 \leq \frac{\pi\rho}{\mu + \omega}.$$

Using this same approach in (9) for (2) to (6), then we have

$S_2(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R_H(0) \geq 0, R(0) \geq 0).$

3.3 Equilibrium Points

To obtain the equilibrium points for the systems of differential equation (2.2) above, by setting each of the equations (1) - (6) to zero.

$$\pi\rho - \mu S_1 - \omega S_1 - \beta S_1 = 0 \tag{3.3.1}$$

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

$$(1-\pi)\rho + \omega S_1 - \mu S_2 - \alpha I S_2 = 0 \tag{3.3.2}$$

$$\beta I S_1 + \alpha I S_2 - \mu E - \sigma E = 0 \tag{3.3.3}$$

$$\sigma E - (\mu + \epsilon) I - \delta I - \gamma I = 0 \tag{3.3.4}$$

$$\delta I - (\mu + \tau) R_H = 0 \tag{3.3.5}$$

$$\gamma I + \tau R_H - \mu R = 0 \tag{3.3.6}$$

The calculating results will be in two equilibrium points, one being the Disease free equilibrium (DFE), while the other being the Endemic equilibrium.

3.3.1 Disease free equilibrium point:

Let the disease free equilibrium of the system of equation (1) - (6) be defined as

$$D_f^0 = (S_1^0, S_2^0, E^0, I^0, R_H^0, R^0)$$

by solving equations (11) - (16), we have,

$$\begin{aligned} D_f^0 =& (S_1^0, S_2^0, E^0, I^0, R_H^0, R^0) \\ =& \left(\frac{\pi\rho}{(\mu+\omega)}, \frac{(1-\pi)\rho(\mu+\omega) + \pi\rho\omega}{\mu(\mu+\omega)}, 0, 0, 0, 0 \right) \end{aligned} \tag{3.3.7}$$

3.3.2 Endemic equilibrium

Let the endemic equilibrium point of the system of equations (1)-(6) be given as:

$$D_f^* = (S_1^*, S_2^*, E^*, I^*, R_H^*, R^*).$$

From equations (11) - (16), let,

$$a = \beta I, b = \alpha I, k_1 = (\mu + \omega + a), k_2 = (\mu + b), k_3 = (\mu + \sigma), k_4 = (\mu + \epsilon + \delta + \gamma), k_5 = (\mu + \tau),$$

we have equations (11) - (16) becomes

$$k_1 S_1 = \pi\rho \tag{3.3.8}$$

$$\omega S_1 - k_2 S_2 = (\pi - 1)\rho \tag{3.3.9}$$

$$a S_1 + b S_2 - k_3 E = 0 \tag{3.3.10}$$

$$\sigma E - k_4 I = 0 \tag{3.3.11}$$

$$\delta I - k_5 R_H = 0 \tag{3.3.12}$$

$$\gamma I + \tau R_H - \mu R = 0. \tag{3.3.13}$$

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

By solving system of equations in (18)-(23), we have the endemic equilibrium as

$$S_1^* = \frac{\pi\rho}{k_1} \tag{3.3.14}$$

$$S_2^* = \frac{\omega\pi\rho - k_1(1-\pi)\rho}{k_1 k_2} \tag{3.3.15}$$

$$E^* = \frac{ak_2\pi\rho + b(\omega\pi\rho - k_1(1-\pi)\rho)}{k_1 k_2 k_3} \tag{3.3.16}$$

$$I^* = \frac{\sigma[ak_2\pi\rho + b(\omega\pi\rho - k_1(1-\pi)\rho)]}{k_1 k_2 k_3 k_4} \tag{3.3.17}$$

$$R_H^* = \frac{\sigma\delta[ak_2\pi\rho + b(\omega\pi\rho - k_1(1-\pi)\rho)]}{k_1 k_2 k_3 k_4 k_5} \tag{3.3.18}$$

$$R^* = \frac{(\tau\sigma\delta + \gamma\sigma k_5)(ak_2\pi\rho + b(\omega\pi\rho - k_1(1-\pi)\rho)}{\mu k_1 k_2 k_3 k_4 k_5} \tag{3.3.19}$$

3.4 Basic Reproduction number (R_0) for DFE

The basic reproduction number is defined as the average number of secondary infections caused by infected individual in a whole population. This can be computed by the method of next generation matrix applied to the equation (3), (4) and (5), and by taking the largest eigenvalue (spectral radius) of FV^{-I}.

Where F is the matrix of infectious rate, defines as $\frac{\partial F_i(x_i)}{\partial(x_i)}$ and V is the matrix of transition rate, defines as $\frac{\partial V_i(x_i)}{\partial(x_i)}, i = 1, 2, 3, ...$

Consider the system in equations (3), (4) and (5) i.e

$$\begin{aligned}
\frac{dE}{dt} &= \beta I S_1 + \alpha I S_2 - \mu E - \sigma E \\
\frac{dI}{dt} &= \sigma E - (\mu + \epsilon) I - \delta I - \gamma I \\
\frac{dR_H}{dt} &= \delta I - (\mu + \tau) R_H
\end{aligned}$$

$$F = \begin{bmatrix} 0 & \beta S_1 + \alpha S_2 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} (\mu+\sigma) & 0 & 0 \\ -\sigma & (\mu+\epsilon+\gamma+\delta) & 0 \\ 0 & -\delta & (\mu+\tau) \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{(\mu+\sigma)} & 0 & 0 \\ \frac{\sigma}{(\mu+\sigma)(\mu+\epsilon+\gamma+\delta)} & \frac{1}{(\mu+\epsilon+\gamma+\delta)} & 0 \\ \frac{\sigma\delta}{(\mu+\sigma)(\mu+\epsilon+\gamma+\delta)(\mu+\tau)} & \frac{\delta}{(\mu+\epsilon+\gamma+\delta)(\mu+\tau)} & \frac{1}{(\mu+\tau)} \end{bmatrix}$$

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

$$FV^{-1} = \begin{bmatrix} \frac{(\beta IS_1+\alpha IS_2)\sigma}{(\mu+\sigma)(\mu+\epsilon+\gamma+\delta)} & \frac{(\beta IS_1+\alpha IS_2}{(\mu+\epsilon+\gamma+\delta)} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

The spectral radius of

$$R_0 = \rho(FV^{-1}) = \frac{(\beta IS_1 + \alpha IS_2)\sigma}{(\mu+\sigma)(\mu+\epsilon+\gamma+\delta)} \tag{3.4.1}$$

$$= \frac{(\mu\beta+\omega\alpha)\pi\rho\sigma + (\mu+\omega)(1-\pi)\rho\alpha\sigma}{\mu(\mu+\sigma)(\mu+\omega)(\mu+\epsilon+\gamma+\delta)} \tag{3.4.2}$$

3.5 Stability Analysis for Disease free equilibrium

In order for us to established the stability of the disease free equilibrium, some certain condition must be meet, either the disease will be totally eradicated or not, from the population. We considered both local and global stability of the disease free equilibrium.

3.5.1 Local Stability of the disease free equilibrium

Theorem 3.3 *The disease free equilibrium of the system (1) to (6) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$ or the disease free equilibrium is locally stable if and only if all the eigenvalues of the Jacobian matrix of the systems are all negatives.*

Proof

By Jacobian, we obtain the matrix of the system at the disease free equilibrium points.

$$J = \begin{bmatrix} -(\mu+\omega+\beta I) & 0 & 0 & \frac{-\pi\beta\rho}{(\mu+\omega)} & 0 & 0 \\ \omega & -\mu & 0 & \frac{-\alpha\rho(\mu+\omega-\mu\pi)}{\mu(\mu+\omega)} & 0 & 0 \\ 0 & 0 & -(\mu+\sigma) & & 0 & 0 \\ 0 & 0 & \sigma & (\mu+\epsilon+\gamma+\delta) & 0 & 0 \\ 0 & 0 & 0 & \delta & -(\mu+\tau) & 0 \\ 0 & 0 & 0 & \gamma & \tau & -\mu \end{bmatrix} \tag{3.5.1}$$

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

Using column reduction, matrix (32) becomes

$$J = \begin{bmatrix} -(\mu+\omega+\beta I) & 0 & \frac{-\pi\sigma\beta\mu\rho(\mu+\tau)}{(\mu+\omega)} & \frac{-\pi\beta\mu\rho(\mu+\tau)}{(\mu+\omega)} & 0 & 0 \\ \omega & -\mu & \frac{-\alpha\rho(\mu+\tau)(\mu+\omega-\mu\pi)}{(\mu+\omega)} & \frac{-\alpha\rho(\mu+\tau)(\mu+\omega-\mu\pi)}{(\mu+\omega)} & 0 & 0 \\ 0 & 0 & -\mu(\mu+\sigma)(\mu+\tau)(\mu+\epsilon+\gamma+\delta) & 0 & 0 & 0 \\ 0 & 0 & 0 & -(\mu+\tau)(\mu+\epsilon+\gamma+\delta) & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu(\mu+\tau) & 0 \\ 0 & 0 & 0 & 0 & 0 & -\mu \end{bmatrix} \tag{3.5.2}$$

Since the resulting matrix is an upper triangular matrix, then the eigenvalues are the diagonal entries of the matrix.

$$\lambda_1 = -(\mu+\omega+\beta I), \lambda_2 = -\mu, \lambda_3 = -\mu(\mu+\sigma)(\mu+\tau)(\mu+\epsilon+\gamma+\delta),$$
$$\lambda_4 = -(\mu+\tau)(\mu+\epsilon+\gamma+\delta), \lambda_5 = -\mu(\mu+\tau), \lambda_6 = -\mu$$

From the above results in equation (33), the disease free equilibrium of the model is locally asymptotically stable since all the eigenvalues are all negatives.
Alternatively,
Consider the basic reproduction number R_0 as in equation (31), for the system to be locally asymptotically stable we need to show that

$$R_0 = \frac{(\mu\beta+\omega\alpha)\pi\rho\sigma + (\mu+\omega)(1-\pi)\rho\alpha\sigma}{\mu(\mu+\sigma)(\mu+\omega)(\mu+\epsilon+\gamma+\delta)} < 1$$

Using values of the parameters in table 4 below, we find out that $R_0 = 0.2604814805$ which is less than 1.
Hence the disease free equilibrium of the model is local asymptotically stable.

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

3.6 Sensitivity Analysis

Sensitivity analysis of the system of the differential equation above is defined as the derivatives of the solution with respect to the parameters. The sensitivity analysis serves two main purposes. On one hand, the sensitivities are diagnostics of the model which are useful for understand how it will change in accordance with changes in the parameters. In order for us to compute the sensitivity index of the above system, we use the partial derivatives of R_0 with respect to each parameter. i.e

$$\gamma_{\mu}^{R_0} = \left| \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} \right|,$$

3.6.1 Parameter Values

Parameter	Value	Unit	Reference
$\pi\rho$	0.25	Person per year	A.A Momoh and A Tahir (2015)
$(1-\pi)\rho$	0.75	Person per year	Assumed
μ	0.0241	Per year	D. Okuonghae (2013)
ω	0.01	Per year	Assumed
β	8.557	Per year	D. Okuonghae (2013)
α	1.5	Per year	D. Okuonghae (2013)
σ	0.001	Per year	A.A Momoh and A Tahir (2015)
δ	0.32	Per year	Assumed
ϵ	3.65	Per year	Assumed
γ	7.5	Per year	Assumed
τ	1.5	Per year	D. Okuonghae (2013)

Table 3: The parameters values from existing literatures and those assumed by the author

3.6.2 Sensitivity Values

Parameter	Value	Security Value
$\pi\rho$	0.25	0.3894544033
$(1-\pi)\rho$	0.75	0.6105455968
μ	0.0241	-0.1812390091
ω	0.01	-0.01498301404
β	8.557	0.2254614952
α	1.5	0.774536313
σ	0.001	0.9601593627
δ	0.32	-0.02736422641
ϵ	3.65	-0.3121232075
γ	7.5	-0.6413490565

Table 4: The computation of sensitivity values for each parameter

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

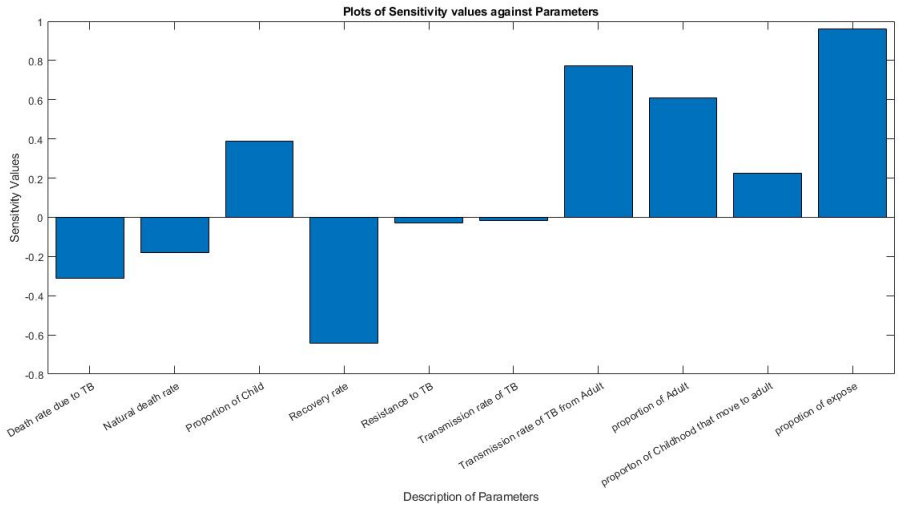

Figure 2: The histogram plot of sensitivity values against parameters

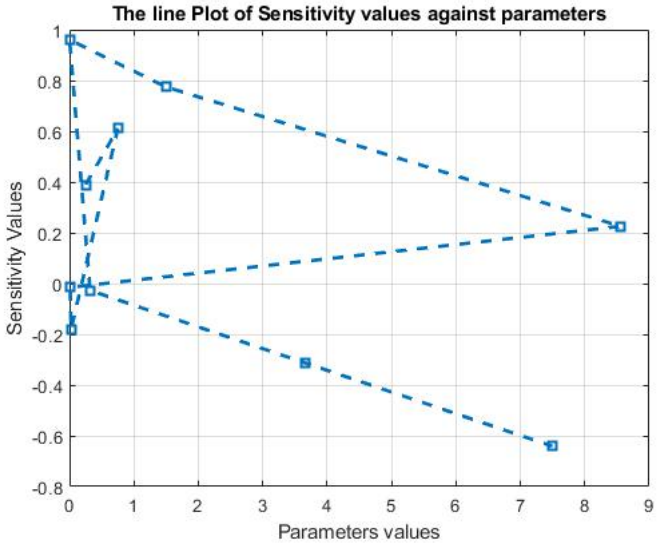

Figure 3: The line plots of Sensitivity values with parameters

3.7 Numerical Solution of the Model

The numerical simulation were carried out with Maple 17 using the parameter values in table 4 above

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

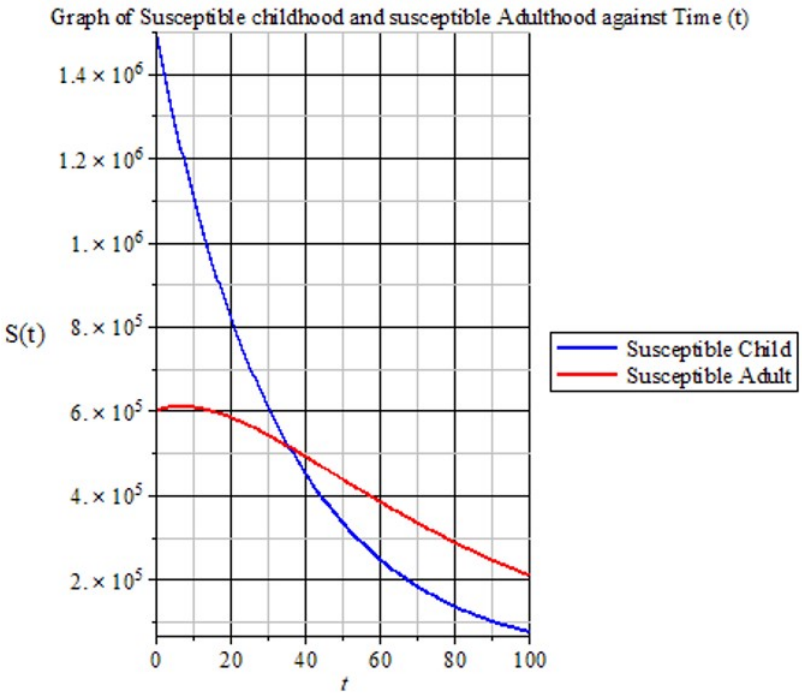

Figure 4: The graph of susceptible population against time in years

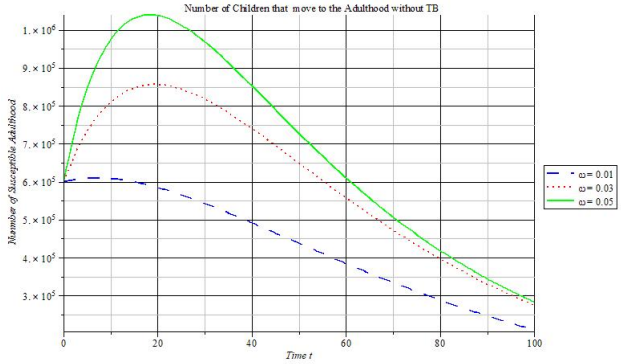

Figure 5: Variation of Child that moves to Adulthood with contact the virus

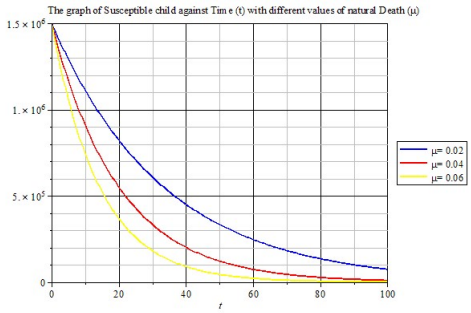

Figure 6: Proportion of Susceptible Childhood with different values of Natural death rate

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
DOI.ORG/10.6084/M9.FIGSHARE.13989374.

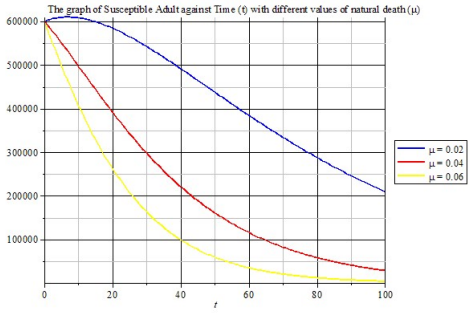

Figure 7:Proportion of Susceptible Adulthood with different values of Natural death rate

Figure 8:Proportion of Exposed Class with different values of Natural death rate

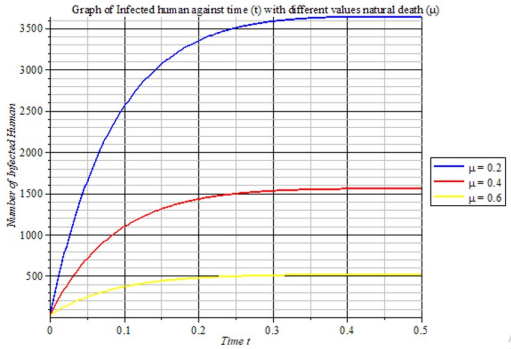

Figure 9: Proportion of people that infected with the disease, with different values of Natural death.

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

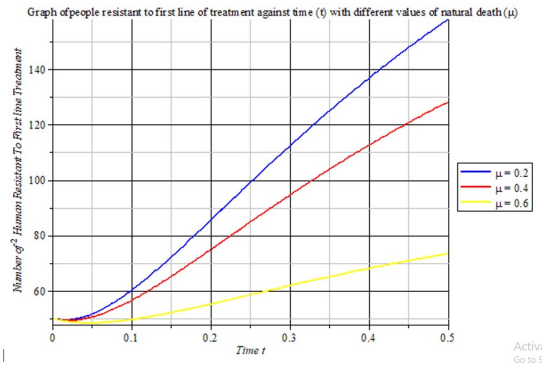

Figure 10: Proportion of peoples with resistant to the first line of treatment,with different values of Natural death rate

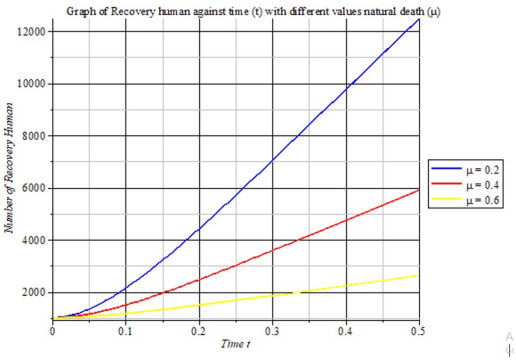

Figure 11: Proportion of people that are recovered from the disease with difference natural death

4 Discussion of Results

In this paper, we established the Sensitivity analysis of mathematical model of Tuberculosis disease with resistance to drug treatment and the following results were obtained
1. The solution to the model are bounded and exist
2. All choosing parameters are epidemiologically meaningful and well posed
3. The disease free equilibrium of the model is locally asymptotically stable.
4. From the Sensitivity Analysis, the positive index indicates an increase in the value of basic reproduction number with increase in the parameter values while negative values indicates decrease in the basic reproduction number with increase in parameter values
5. The sensitivity analysis show that the most sensitivity parameter is the contact rate σ (The rate at which the human get infected with the tuberculosis.

5 Conclusion

A model of six compartment was developed. The equilibrium point of the model was calculated (Disease free and Endemic Equilibrium). The local stability were obtained and analysed based on the basic reproduction number of the model and it was observed that the model is locally asymptotically stable. The sensitivity analysis show that the most sensitivity parameter is the contact rate σ (The rate at which the human get infected with the tuberculosis).It was observed that the age group has bigger effect on the control of TB. The drug resistance has a little effect on the total control of the disease. At the end, three effective measure was found that would help reach

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

the major goal of the WHO End the Strategy: reduce the exposed rate of the disease especially in the adults, increase the recovery rate and reduce the transmission rate of the adults.

Acknowledgements

Authors are grateful to the reviewer and managing editor for their constructive comments. we equally appreciate the Research Group in Mathematics and Application(RGMA) whose the author is a member.
In Memory of My Co-Author: I will like to dedicate this work to Almighty God, to whom all things are possible, and my Co-Author and Mentor, Late Professor Folake Akinpelu, for her immense support toward this work.

Competing financial interests

The author declares no competing financial interests.

References

[1] Liu,L. & Wang,Y. A mathematical study of a TB model with treatment interruptions and two latent periods. *Computational and mathematical methods in medicine* **2014**, (2014).

[2] Okuonghae,D. & Ikhimwin,B.O. Dynamics of a mathematical model for tuberculosis with variability in susceptibility and disease progressions due to difference in awareness level. *Frontiers in microbiology* **6**, 15–30, (2016).

[3] Waaler,H., Geser,A. & Andersen,S. The use of mathematical models in the study of the epidemiology of tuberculosis. *American Journal of Public Health and the Nations Health* **52**, 1002–1013 (1962).

[4] Ronoh,M., Jaroudi,R., Fotso,P., Kamdoum,V., Matendechere,N., Wairimu,J., Auma,R. & Lugoye,J. A mathematical model of tuberculosis with drug resistance effects. *Applied Mathematics* **7**, 1303–1316, (2016).

[5] Yu,Y., Shi,Y. & Yao,W. Dynamic model of tuberculosis considering multi-drug resistance and their applications. *Infectious Disease Modelling* **3**, 362–372, (2018).

[6] Gupta,V.K., Tiwari,S.K., Sharma,S. & Nagar,L. Mathematical model of tuberculosis with drug resistance to the first and second line of treatment. *Journal of New Theory* **21**, 94–106, (2018).

[7] Fofana,M.O., Shrestha,S., Knight,G.M., Cohen,T., White,R.G., Cobelens,F. & Dowdy,D.W. A multistrain mathematical model to investigate the role of pyrazinamide in the emergence of extensively drug-resistant tuberculosis. *Antimicrobial agents and chemotherapy* **61**, 90–100, (2017).

[8] Ozcaglar,C., Shabbeer,A., Vandenberg,S.L., Yener,B. & Bennett,K.P. Epidemiological models of Mycobacterium tuberculosis complex infections. *Mathematical Biosciences* **236**, 77–96, (2012).

[9] McCluskey,C.C. & Vanden,D.P. Global analysis of two tuberculosis models. *Journal of Dynamics and Differential Equations* **16**, 589–598, (2004).

[10] World Health Organization World malaria report 2015. *World Health Organization* (2016).

IJMSO

International Journal of Mathematical Sciences and Optimization: Theory and Applications
Vol. 6, No. 2, pp. 939 - 954.
doi.org/10.6084/m9.figshare.13989374.

[11] Annabel,B., Anna,D. & Hannah,M. Global tuberculosis report 2019. *Geneva: World Health Organization* (2019).

[12] Greenhalgh,D., Rana,S., Samanta,S., Sardar,T., Bhattacharya,S. & Chattopadhyay,J. Awareness programs control infectious disease–multiple delay induced mathematical model. *Applied Mathematics and Computation* **251**, 539–563, (2015).

[13] Omale,D., Atokolo,W. & Akpa, M. Mathematical Modeling of the Transmission Dynamics of Tuberculosis and its Control. (A case study of Ika General Hospital, Ankpa, Kogi State). *IOSR Journal of Mathematics* **15**, 37–47, (2019).

[14] Omale,D., Atokolo,W. & Akpa,M. Sensitivity Analysis of Transmission Dynamics of Tuberculosis and its Control. (A case study of Ika General Hospital, Ankpa, Kogi State. *Academic Journal of Statistics and Mathematics (AJSM)* **6**, 1–14, (2020).