



## A Mathematical Model of Tuberculosis with Passive Immunity and Drug Resistance Effects

M. Abdullahi<sup>1</sup>, A. A. Momoh<sup>1\*</sup>, S. A. Abdullahi<sup>1</sup> and H. O. Edogbanya<sup>2</sup>

<sup>1</sup>Department of Mathematics, Modibbo Adama University of Technology, Yola, Adamawa State, Nigeria

<sup>2</sup>Department of Mathematical Science, Federal University Lokoja, Kogi State, Nigeria

Corresponding Authors Email: [abdulfatai@mautech.edu.ng](mailto:abdulfatai@mautech.edu.ng)

Received on: November 2018

Revised and Accepted on: September 2019

### ABSTRACT

Despite the enormous progress in prevention and treatment, tuberculosis remains a leading cause of death worldwide. One of the major sources of concern is the drug resistant strain, MDR-TB (Multidrug Resistant Tuberculosis) and XDR-TB (Extensively Drug Resistant Tuberculosis). In this paper we present an extension of the SEIRS epidemiology model of tuberculosis by incorporating passive immunity and MDR-TB. We analyzed the local stability of the disease free equilibrium (DFE) point using the next generation method. The result shows that the DFE point is locally asymptotically stable whenever  $R_0 < 1$  and unstable whenever  $R_0 > 1$ . Furthermore, we constructed a Lyapunov for the global stability of DFE. The result revealed that the disease free equilibrium point is globally asymptotically stable whenever  $R_0 \leq 1$ . The numerical simulation of the model was carried out to show the effects of drug resistant and passive immunity on the transmission dynamics of Tuberculosis. We conclude that, efficacy of drugs ought to be improved and second line of treatment should be enforced in order to control Tuberculosis.

**Keywords:** Multidrug Resistant Tuberculosis, Passive Immunity, Basic Reproduction Number, Stability, Epidemiology

### 1. INTRODUCTION

Tuberculosis is an airborne disease caused by *Mycobacterium tuberculosis* (MTB) bacteria (Daniel, 2006). It is an ancient disease with evidence of its existence being found in relics from ancient Egypt, India and China (Daniel, 2006). In the eighteenth century, Western Europe suffered terribly from this disease with prevalence as high as 900 deaths per 100,000. This was largely due to poor ventilation, overcrowded housing, primitive sanitation and malnutrition among other risk factors that led to the epidemic (Daniel, 2006). Today, this disease ranks as the second leading cause of morbidity and mortality in the world after the human immunodeficiency virus (HIV) (WHO, 2014). Interestingly, about one-third of the world's

population is infected with MTB. Approximately nine million people are developing active tuberculosis and up to nearly two million people worldwide die from the disease every year. In 2013, approximately nine million people contracted active tuberculosis and this included 1.1 million cases among people living with HIV and 550,000 children. Out of these nine million cases 1.5 million people succumbed to the disease and this included 360,000 among people who were HIV-positive, 510,000 were women out of which 180,000 were HIV-positive. Africa recorded the highest tuberculosis/HIV burden with three out of four Tuberculosis patients knowing their HIV status. Approximately 480,000 people developed multidrug-Resistant (MDR) tuberculosis

globally with 210,000 of those who developed MDR tuberculosis succumbing to it (WHO, 2014). In 2015, there were an estimated 10.4 million new (incident) TB cases worldwide, of which 5.9 million (56%) were among men, 3.5 million (34%) among women and 1.0 million (10%) among children. People living with HIV accounted for 1.2 million (11%) of all new TB cases (WHO, 2016). Six countries accounted for 60% of the new cases: India, Indonesia, China, Nigeria, Pakistan and South Africa. Global progress depends on major advances in TB prevention and care in these countries. Worldwide, the rate of decline in TB incidence remained at only 1.5% from 2014 to 2015. This needs to be accelerated by 4–5% annual decline by the year 2020 to reach the first milestones of the End TB Strategy (WHO, 2014). In addition to posing a major health concern to low and middle-income countries, tuberculosis affects economic growth negatively (Klein, Laxminarayan, Smith, and Gilligan, 2007).

Psychosocial distress that communities go through is enormous. This involves thinking about the loss of their loved ones and the economic impact of taking care of the sick ones especially among the low-income individuals. This affect not only the individuals, but also the economic progress of the country. Over the last twenty-five years, the mortality rate of tuberculosis has greatly decreased by forty five percent since and this is largely due to effective diagnosis and treatment (Semenza, Suk, and Tsoleva, 2010). However, the world is still far from defeating the disease. About 8 billion US dollars per year is needed for a full response to the global tuberculosis epidemic in low and middle-income countries by the year 2015 with a funding gap of 2 billion US dollars per year.

This amount excluded resources required for research and development, which was estimated to be about 2 billion US dollars yearly (WHO, 2014). Clearly, this reveals that the current investment in tuberculosis falls below the low and middle-income country's needs. (MTB) bacteria spread through inhaling droplets from the cough or sneeze of a person suffering from active tuberculosis. The bacteria enters the body causing an MTB infection affecting majorly the

lungs but it can also affect any other part of the body including the urinary tract, brain, lymph nodes, bones, joints and the ear. Person(s) with lowered immunity such as those with HIV, diabetes, immune disorders, end-stage renal disease, those on drugs that suppress immunity, young children and pregnant women among others are at a higher risk of contracting the disease (Mandal, 2013). Also people suffering from malnutrition due to lifestyle, drug abuse or poverty equally are at risk of contracting tuberculosis. Another category of people largely at risk of contracting tuberculosis are those who work closely or live close to a person with active tuberculosis and they could include health care workers, people living in crowded living spaces or confined places such as schools or prisons (Zaman, 2010). The intensity of transmission depends on factors related to the bacteria, the human host, the environment and migration. Non-climatic factors such as environmental development and urbanization, population movement and migration affect the severity and incidence of tuberculosis. When it comes to environment and urbanization, the incidence of tuberculosis is generally lower in prime urban areas than in rural areas as there is difficulty in accessing proper medical care in rural villages compared to urban areas. However, rapid urbanization of areas within or on the outskirts of urban centers is commonly done in an uncontrolled fashion without thought or planning. The settlers are mainly migrant workers from rural villages and they tend to settle mostly in poor, overcrowded houses commonly known as slums with hardly any proper sanitation and this in turn leads to increased exposure of the population to MTB hence, a possibility of amplification of the disease to epidemic proportions through lack of effective treatment (Mandal, 2013). Population movements have significant implications for tuberculosis transmission as migration introduces tuberculosis problem to the areas to which the migrants migrate to. Temporary migrant workers often bring the bacteria to lower prevalence areas and local transmission can be readily established (Semenza, Suk, and Tsoleva, 2010). Tuberculosis is curable provided an early diagnosis is made and one follows the proper treatment regimen which could take six

months up to two years for the active tuberculosis to clear (Trauer, Denholm, MCBryde, 2014). There is an emerging form of tuberculosis commonly known as multi-drug resistant (MDR) tuberculosis which is defined as tuberculosis resistant to both of the two most effective first line of antibiotic treatment of active tuberculosis *i.e.*, isoniazid (INH) and rifampin (RIF), and it is harder and more expensive to treat. It is currently a major health concern to medical workers and researchers and one can get MDR tuberculosis by either spending time with an MDR patient or breathing in the MDR tuberculosis bacteria or those with active tuberculosis not following their prescribed treatment regimen or TB medicine not being readily available to them. MDR tuberculosis is much more difficult to treat and the mortality of persons with this form of tuberculosis is far much higher if the second line of antibiotic treatment is not effected promptly (Mandal, 2013). Waaler, and Anderson(1962) developed a mathematical model to study the epidemiology of tuberculosis. With time other models have been developed to help prevent the risk of transmission of tuberculosis (Castillo-Chavez, and Feng, 2009). Recent global reports of multidrug resistant and extensively drug-resistant tuberculosis have renewed concerns that antibiotic resistance may undermine progress in tuberculosis control (Young, Stark,Kirschner, 2008). Including MDR tuberculosis in mathematical models is relatively new and there are very few models with this aspect. Agosto, Cook, Shelton, and Wicker (2015) used a deterministic model with isolation where they studied the transmission dynamics of three strains of mycobacterium tuberculosis (TB), namely; the drug sensitive, multi-drug-resistance (MDR) and extensively-drug-resistance (XDR) tuberculosis strains. The result of the global sensitivity analysis indicated that the dominant parameters are the disease progression rate, the recovery rate, the infectivity parameter, the isolation rate, and the rate of cost to follow up and fraction of fast progression rates. They also found that an increase in isolation rate leads to a decrease in the total number of individuals who are cost to follow up. Trauer, Denholm and McBryde(2014) used a mathematical model to simulate

tuberculosis transmission in the highly endemic regions of the Asia-pacific. They found out that their model could not be calibrated to the estimated incidence rate without allowing for re-infection during latency and that even in the presence of a moderate fitness cost and a lower value of  $R_0$ , MDR tuberculosis becomes the dominant strain at equilibrium. Improved treatment of drug susceptible tuberculosis did not result in decreased rates of MDR tuberculosis through prevention of the new resistance but rather resulted in a modest increase in MDR tuberculosis. (Cohen, and Murray, 2014) modeled epidemics of multi-drug resistant tuberculosis of heterogeneous fitness. Their model suggested that the threat of multidrug resistance to tuberculosis control depends on relative fitness of MDR strains and this implied that the strains is considerably less than that of drug-sensitive strains and that the emergence of resistance would not jeopardize the success of tuberculosis control efforts. Their results implied that current epidemiological measures and short- term trends in the burden of MDR tuberculosis do not provide evidence that MDR tuberculosis strains can be contained in the absence of specific efforts to limit transmission from those with MDR disease. In 2015, there were an estimated 480, 000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100, 000 people with rifampicin-resistant TB (RR-TB) who were also newly eligible for MDR-TB treatment. India, China and the Russian Federation accounted for 45% of the combined total of 580, 000 cases (WHO, 2016).

## 2. MODEL FORMULATION

The total population is categorized into six time dependent classes namely, the passive immune infants  $M$ , susceptible individuals  $S$ , exposed individuals to tuberculosis  $E$ , infected individuals with active tuberculosis  $I$ , resistant individuals to the first line of treatment  $R_{ES}$  and recovered individuals is represented by  $R$ . Thus, the total population is given as;

$$N = M + S + E + I + R_{ES} + R$$

The passive immune class is increases by birth with passive immunity (at a rate  $(1 - P)\lambda$ ) and

decreases by natural death (at a rate  $\mu$ ) and by those passive immune infants whose immunity wanes out (at a rate  $\eta$ ). The susceptible population increases by birth without passive immunity (at a rate  $P\lambda$ ). This class is further increased by the passive immune infants who loses immunity (at a rate  $\eta$ ) and recovered individuals that becomes susceptible again (at the rate  $\rho$ ). The susceptible class decreases by natural death (at a rate  $\mu$ ) and the infection of the susceptible individuals (at a rate  $\beta$ ). The population of exposed class is generated by the infection of the susceptible individuals (at a rate  $\beta$ ). Natural death (at a rate  $\mu$ ) and the proportion that move to the infected class after developing active tuberculosis decreases the exposed class. The infected class is generated by progression from the exposed class who become infectious i.e. those who

developed active tuberculosis (at a rate  $\varepsilon$ ). This class is reduced by natural death (at a rate  $\mu$ ), disease induced death (at a rate  $\alpha$ ), those who recover from active TB (at a rate  $\gamma$ ) and also by those who become resistant to the first line of treatment (at a rate  $\sigma$ ). The resistant class is generated by those who become resistant to the first line of treatment (at a rate  $\sigma$ ) and this population reduces by natural death (at rate  $\mu$ ), disease induced death (at a rate  $\alpha_1$ ) and by those who gain partial immunity (at a rate  $\delta$ ). The recovered class increases by those who acquire partial immunity in the infected and resistant classes at the rates  $\gamma$  and  $\delta$  respectively. The natural death (at a rate  $\mu$ ) and those who lose immunity (at a rate  $\rho$ ) reduce the recovered class. The description of the state variables and parameters are presented in Table 1 and Table 2.

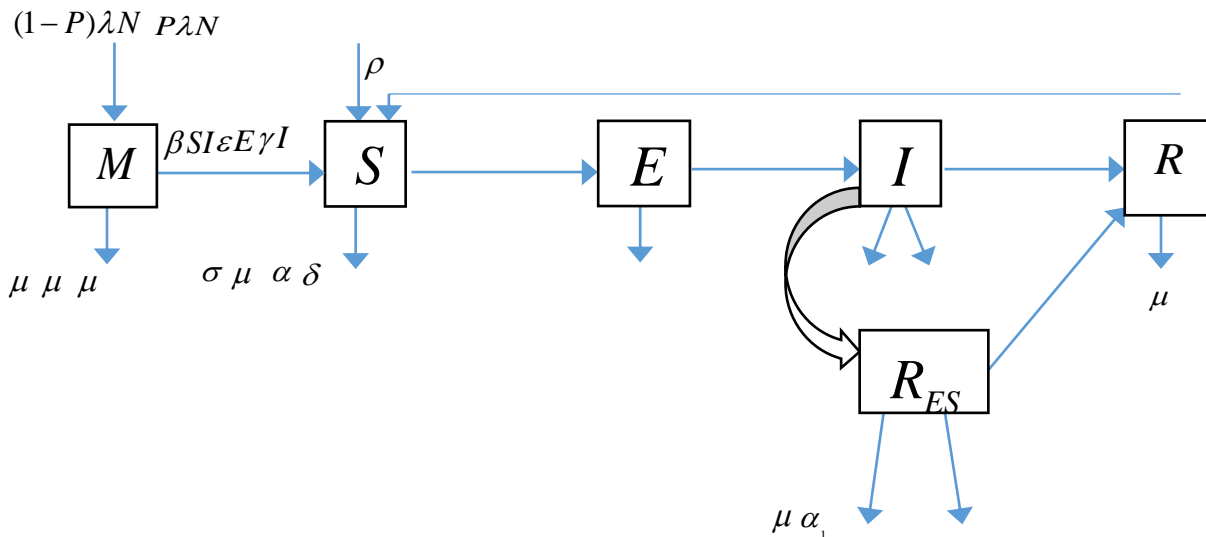


Figure 1. Schematics of the compartmental model

Table 1: Description of State Variables

Variable	Description
$N(t)$	Total Population
$M(t)$	Number of Passive immune infants at time t
$S(t)$	Number of Susceptible individuals at time t
$E(t)$	Number of Exposed individuals at time t
$I(t)$	Number of Infectious individuals at time t
$R(t)$	Number of Recovered individuals from both active and MDR Tuberculosis (TB) at time t

$R_{ES}(t)$  Number of Resistant individuals to first line of treatment at time t

**Table 2: Description of Parameters**

Parameter	Description
$\lambda$	Birth rate
$P$	Proportion of infants without passive immunity
$\eta$	Rate at which passive immune infants become susceptible
$\beta$	Transmission rate
$\sigma$	Resistant rate to treatment
$\mu$	Death rate
$\varepsilon$	Progression rate
$\gamma$	Recovery rate of active TB
$\alpha$	Disease induced death rate due to active TB
$\alpha_1$	Disease induced death rate due to MDR TB
$\delta$	Recovery rate of infected individuals from MDR TB
$\rho$	Rate of loss of immunity by recovered individuals

Thus, from the descriptions and the schematics of model we derived the following model equations.

$$\left. \begin{aligned} \frac{dS}{dt} &= P\lambda N + \eta M - \beta SI - \mu S + \rho R \\ \frac{dM}{dt} &= (1-P)\lambda N - (\mu + \eta)M \\ \frac{dE}{dt} &= \beta SI - (\mu + \varepsilon)E \\ \frac{dI}{dt} &= \varepsilon E - (\mu + \alpha + \gamma + \sigma)I \\ \frac{dR_{ES}}{dt} &= \sigma I - (\mu + \alpha_1 + \delta)R_{ES} \\ \frac{dR}{dt} &= \gamma I - (\mu + \rho)R + \delta R_{ES} \end{aligned} \right\} \quad (1)$$

### 3.0 MODEL ANALYSIS

#### 3.1 Disease-Free Equilibrium Point (DFE)

The Disease-Free Equilibrium (DFE) points of the model is

$$\Psi^0 = (M^0, S^0, E^0, I^0, R_{ES}^0, R^0) = \left( \frac{(1-P)\lambda N}{\mu + \eta}, \frac{P\lambda N(\mu + \eta) + \eta\lambda N(1-P)}{\mu^2 + \mu\eta}, 0, 0, 0, 0 \right) \quad (2)$$

### 3.2 Endemic Equilibrium Point

The Endemic Equilibrium (EE) points of the model is

$$\psi^* = \left. \begin{aligned} M^* &= \frac{(1-P)\lambda N}{\mu + \eta} \\ S^* &= \frac{(\mu + \varepsilon)(\mu + \alpha + \sigma + \gamma)}{\beta\varepsilon} \\ I^* &= \frac{\tau\varepsilon(Q(\mu + \eta) - \mu\phi(\mu + \eta) + \eta\beta\varepsilon(1-P)\lambda N)}{\beta\varepsilon(\mu + \eta)(\tau\phi - x\varepsilon)} \\ E^* &= \frac{(\mu + \alpha + \gamma + \delta)}{\varepsilon} \frac{\tau\varepsilon(Q(\mu + \eta) - \mu\phi(\mu + \eta) + \eta\beta\varepsilon(1-P)\lambda N)}{\beta\varepsilon(\mu + \eta)(\tau\phi - x\varepsilon)} \\ R_{ES}^* &= \frac{\sigma\tau\varepsilon(Q(\mu + \eta) - \mu\phi(\mu + \eta) + \eta\beta\varepsilon(1-P)\lambda N)}{\beta\varepsilon(\mu + \alpha_1 + \delta)(\mu + \eta)(\tau\phi - x\varepsilon)} \\ R^* &= \frac{\gamma + \sigma\delta}{(\mu + \rho)} \frac{\tau\varepsilon(Q(\mu + \eta) - \mu\phi(\mu + \eta) + \eta\beta\varepsilon(1-P)\lambda N)}{\beta\varepsilon(\mu + \eta)(\tau\phi - x\varepsilon)} \end{aligned} \right\} \quad (3)$$

Where:  $f = (m + e)(m + a + s + d), \quad x = r(g(m + a_1 + d) + sd)$

$$Q = P\lambda N\beta\varepsilon, \quad \tau = (\mu + \rho)(\mu + \alpha_1 + \delta)$$

### 3.3 Local Stability of the Disease Free Equilibrium (DFE)

The local stability of the disease free equilibrium (DFE) point of the model (1) is determined by the reproduction number  $R_0$ .

The reproduction number  $R_0$  is defined as the average number of secondary cases arising from an average primary case in an entirely susceptible population over the period of infection. We use the method of next generation matrix given by (Diekmann, and Heesterbeek, 2000) and (Van Den Driessche, and Watmogh, 2002) to compute the basic reproduction number  $R_0$ . Considering the infected classes in system (1). Let  $F_i$  be the

rate of appearance of new infection in the  $i$  compartment and  $V_i$  be the rate of transfer of individuals out of compartment  $i$ , given the disease free equilibrium point,  $\Psi^0$ , then  $R_0$  is the spectral radius (largest eigenvalues) of the next generation matrix denoted by

$$R_0 = \rho(FV^{-1}) \quad \text{where} \quad F = \left[ \frac{\partial F_i(\Psi^0)}{\partial x_j} \right] \text{ and}$$

$$V = \left[ \frac{\partial V_i(\Psi^0)}{\partial x_j} \right]$$

The matrices  $F$  and  $V$  for the new infection terms and remaining transfer terms at disease free equilibrium point,  $\Psi^0$  are given by;

$$F = \begin{bmatrix} 0 & \beta \left[ \frac{P\lambda N(\mu + \eta) + \eta\lambda N(1 - P)}{\mu^2 + \mu\eta} \right] & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} (\mu + \varepsilon) & 0 & 0 \\ -\varepsilon & (\mu + \alpha + \gamma + \sigma) & 0 \\ 0 & -\sigma & (\mu + \alpha_1 + \delta) \end{bmatrix}$$

Now taking the inverse of matrix  $V$ , we have

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu + \varepsilon} & 0 & 0 \\ \frac{\varepsilon}{(\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma)} & \frac{1}{(\mu + \alpha + \gamma + \sigma)} & 0 \\ \frac{\varepsilon\sigma}{(\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma)(\mu + \alpha_1 + \delta)} & \frac{\sigma}{(\mu + \alpha + \gamma + \sigma)(\mu + \alpha_1 + \delta)} & \frac{1}{(\mu + \alpha_1 + \delta)} \end{bmatrix}$$

Therefore, the largest eigenvalue of  $FV^{-1}$  is the basic reproduction number,  $R_0$ . Thus, the reproduction number for the model is

$$R_0 = \frac{\beta\varepsilon [P\lambda N(\mu + \eta) + \eta\lambda N(1 - P)]}{(\mu^2 + \mu\eta)(\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma)} \tag{4}$$

Thus, using the approach in (Van Den Driessche, and Watmough, 2002) the following result is established.

**Theorem 1:**

The disease free equilibrium point  $\Psi^0$  of the model (1) is locally asymptotically stable whenever  $R_0 < 1$  and unstable whenever  $R_0 > 1$ .

**3.4 Global Stability of the Disease Free Equilibrium**

We shall apply the theory of Lasalle-Lyapunov function  $V$ , to show the global stability of the disease free equilibrium point given by  $(E, I, R_{ES}) = (0, 0, 0)$ .

**Theorem 2:**

If  $R_0 \leq 1$ , then the disease-free equilibrium  $(E, I, R_{ES}) = (0, 0, 0)$  of the system (1) is globally asymptotically stable on  $\Omega$ .

Where  $\Omega$  is a biological feasible region define as

$$\Omega = (M, S, E, I, R_{ES}, R_H \in \mathbf{R}^6 : M + S + E + I + R_{ES} + R_H = N)$$

**Proof:**

We construct the following Lasalle-Lyapunov function  $V(E, I, R_{ES})$  on the positively invariant compact set  $\Omega$ . Thus on  $\Omega$ ,  $V(E, I, R_{ES})$  is continuous and non-negative.

We define  $V(E, I, R_{ES}) = \varepsilon E + (\mu + \varepsilon)I$ .

Consider the system of ordinary differential equations given by

$$\frac{dE}{dt} = \beta SI - (\mu + \varepsilon)E$$

$$\frac{dI}{dt} = \varepsilon E - (\mu + \alpha + \gamma + \sigma)I$$

(6)

The above system can be written as

$$\frac{dR_{ES}}{dt} = \sigma I - (\mu + \alpha_1 + \sigma)R_{ES}$$

$$\begin{pmatrix} \dot{E} \\ \dot{I} \\ \dot{R}_{ES} \end{pmatrix} = \begin{pmatrix} -(\mu + \varepsilon) & \beta S & 0 \\ \varepsilon & -(\mu + \alpha + \gamma + \sigma) & 0 \\ 0 & \sigma & -(\mu + \alpha_1 + \delta) \end{pmatrix} \begin{pmatrix} E \\ I \\ R_{ES} \end{pmatrix}$$

$$\begin{pmatrix} \dot{E} \\ \dot{I} \\ \dot{R}_{ES} \end{pmatrix} = \begin{pmatrix} -(\mu + \varepsilon) & \beta \left[ \frac{(\mu + \eta)P\lambda N + \eta\lambda N(1-P)}{\mu^2 + \mu\eta} \right] & 0 \\ \varepsilon & -(\mu + \alpha + \gamma + \sigma) & 0 \\ 0 & \sigma & -(\mu + \alpha_1 + \delta) \end{pmatrix} \begin{pmatrix} E \\ I \\ R_{ES} \end{pmatrix}$$

This can be written as  $\dot{W} = A(W)$  where  $A = \begin{pmatrix} -(\mu + \varepsilon) & \beta S & 0 \\ \varepsilon & -(\mu + \alpha + \gamma + \sigma) & 0 \\ 0 & \sigma & -(\mu + \alpha_1 + \delta) \end{pmatrix}$

and  $W = \begin{pmatrix} E \\ I \\ R_{ES} \end{pmatrix}$ . If we define  $V^T = [\varepsilon, \mu + \varepsilon]$ , then the derivative along the trajectories is given by

$\dot{V} = V^T A(I)$  as

$$V^T A(W) = [\varepsilon, \mu + \varepsilon, 0] \begin{bmatrix} -(\mu + \varepsilon) & \beta \left[ \frac{(\mu + \eta)P\lambda N + \eta\lambda N(1-P)}{\mu^2 + \mu\eta} \right] & 0 \\ \varepsilon & -(\mu + \alpha + \gamma + \sigma) & 0 \\ 0 & \sigma & -(\mu + \alpha_1 + \delta) \end{bmatrix}$$

$$= \begin{bmatrix} 0 \\ \varepsilon\beta \left[ \frac{(\mu + \eta)P\lambda N + \eta\lambda N(1-P)}{\mu^2 + \mu\eta} \right] - (\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma) \\ 0 \end{bmatrix}$$

$$= \begin{bmatrix} 0 \\ (\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma)(R_0 - 1) \\ 0 \end{bmatrix}$$

Which is strictly decreasing when  $R_0 < 1$ .

Thus  $\dot{V} \leq (\mu + \varepsilon)(\mu + \alpha + \gamma + \sigma)(R_0 - 1)$ .

We define the set

$$E = \{(E, I, R_{ES}) \mid E, I, R_{ES} = 0\}.$$

The largest invariant set is contained in the set  $E$  for which  $E = 0, I = 0, \text{ or } R_{ES} = 0$ . Thus

$\dot{V} < 0$  when  $R_0 < 1$ . If  $I = 0$  or  $R_0 = 1$  then

$\dot{V} = 0$ . Thus, by Lasalle's Invariance Principle, the disease free equilibrium point is globally asymptotically stable and hence the end of the proof.

#### 4. NUMERICAL SIMULATIONS

In this section we carry out numerical simulations of the model to study the effects of loss of immunity and drug resistance on the transmission dynamics of Tuberculosis. The numerical solutions of the model was solved by the inbuilt fourth order Runge-Kutta scheme in MATLAB version 8.5. The simulations were run in an interval of 100 years, to assess the effects of drug resistant and the loss of immunity on the populations. The initial values of the state variables and parameters used in the simulations are presented in table 3 and table 4 respectively.

**Table 3: Initial values of the state variables**

Variables	Definition	Values
$S(0)$	Initial value of susceptible individuals	$15 \times 10^3$
$M(0)$	Initial value of passive immune infants	$5 \times 10^3$
$E(0)$	Initial value of exposed individuals	$4 \times 10^3$
$I(0)$	Initial value of infected individuals	$1 \times 10^3$
$R_{ES}(0)$	Initial value of resistant individuals	$1 \times 10^3$
$R(0)$	Initial value of recovered individuals	$1 \times 10^3$

**Table 4: Initial values of the parameters**

Parameter	Definition	Values
$\beta$	Transmission rate	0.35 per year
$\varepsilon$	Progression rate	0.25 per year
$\alpha$	Disease induced death rate due to active TB	0.01 per year
$\gamma$	Recovery rate of active TB	0.5 per year
$\alpha_1$	Disease induced death rate due to MDR TB	0.0575 per year
$\sigma$	Resistant rate to treatment	0.00 – 0.70 per year
$\delta$	Recovery rate of infected individuals from MDR TB	0.1106456 per year
$\rho$	Rate of loss of immunity by recovered individuals	0.05 per year
$\mu$	Death rate	0.019896 per year
$\eta$	Loss of passive immunity rate	0.00 – 0.45 per year
$P$	Proportion of infants without passive immunity	0.025 per year
$\lambda$	Birth rate	0.045 per year

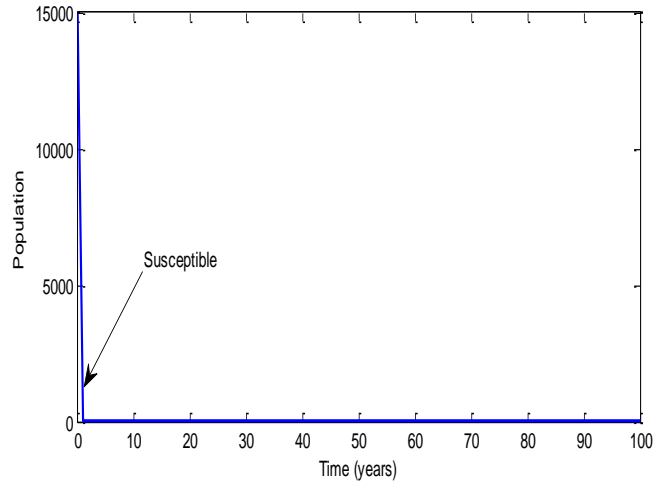


Figure 4.1: Showing simulation for susceptible class

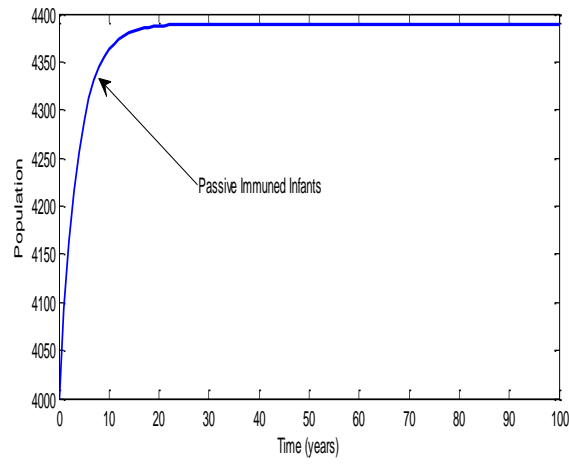


Figure 4.2: Showing simulation for passive immune infants

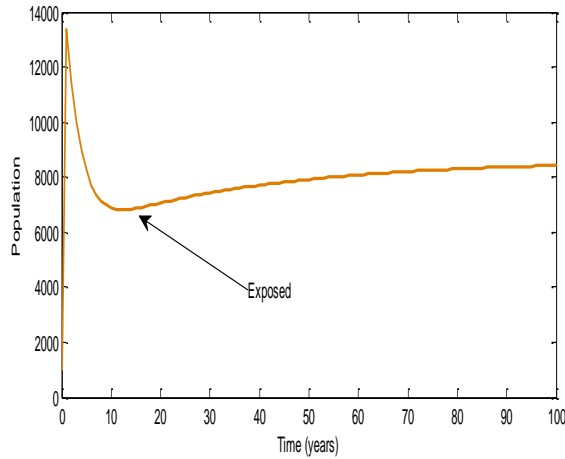


Figure 4.3: Showing simulation for exposed class

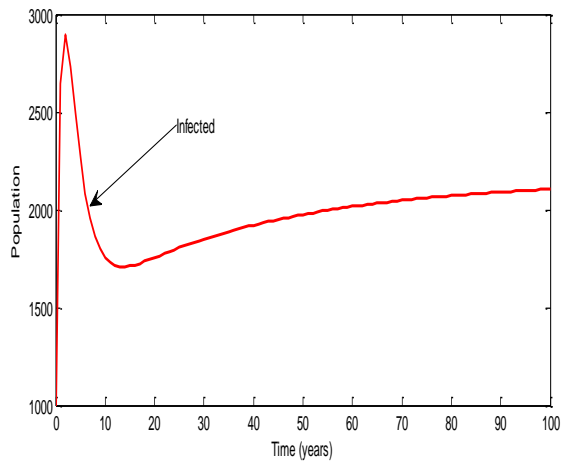


Figure 4.4: Showing simulation for infected class

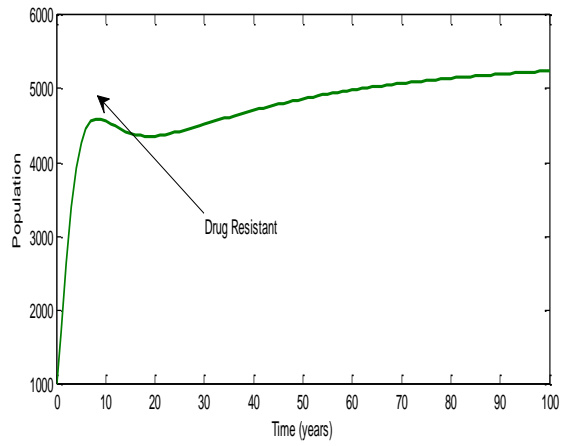


Figure 4.5: Showing simulation for drug resistance class

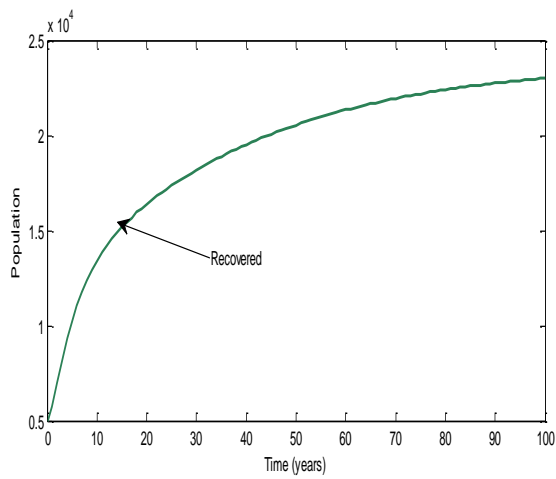
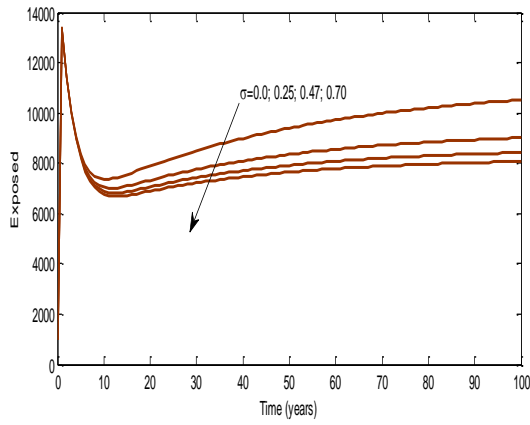
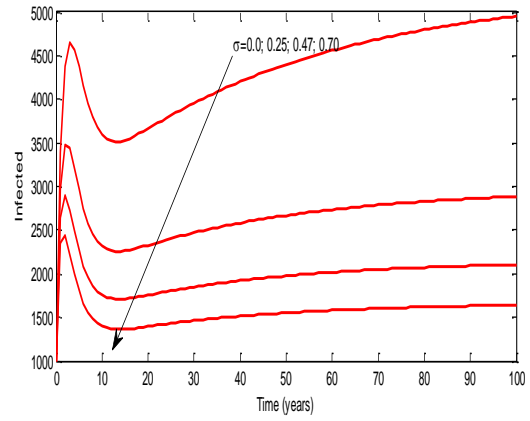


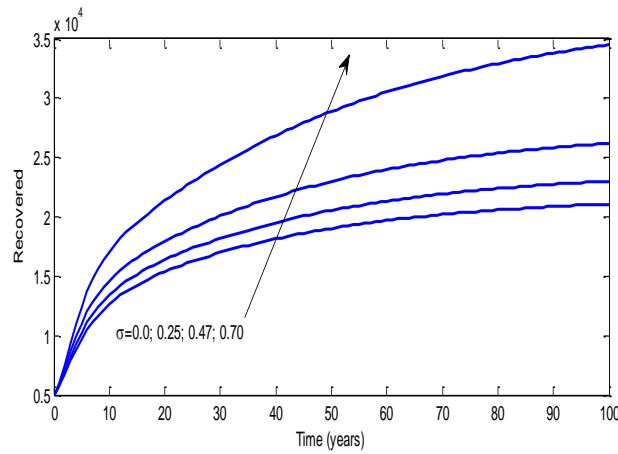
Figure 4.6: Showing simulation for recovered class



(a) Exposed class

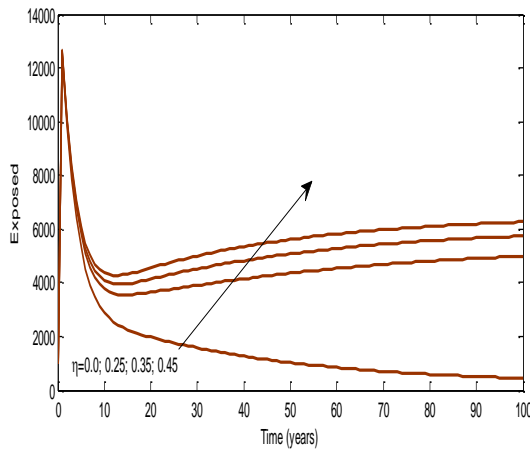


(b) Infected class

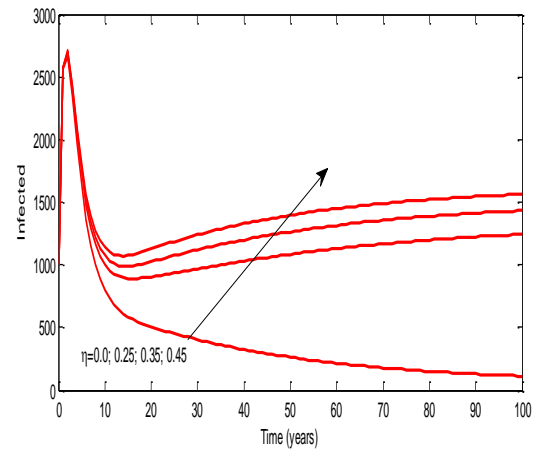


(c) Recovered class

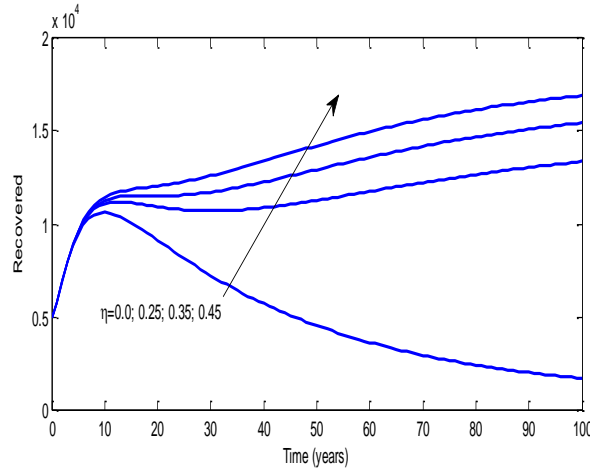
Figure 4.7: Varying drug resistance rate  $\sigma$  between 0.00 and 0.70.



(a) Exposed class



(b) Infected class



(c) Recovered class

Figure 4.8: Varying loss of passive immunity rate  $\eta$  between 0.00 and 0.45

**5. DISCUSSION OF RESULT**

In this section we discuss numerical results depict in figure (4.1) to figure (4.8). Figure (4.1) to figure (4.6) shows the numerical solutions of the model in the presence of drug resistance and loss of passive immunity. Figure (4.1) shows a drastic decrease in the population of susceptible while the passive immune infants' increases and later remain constant for the remaining years, this is shown in figure (4.2). The population of exposed individuals in the presence of drug resistant shows a rapid increase and later decline and stabilizes see figure (4.3). In figure (4.4) we observe a sharp increase of infected population in the presence of drug resistance and after the fifth year there was a significant decline. From the 10<sup>th</sup> year constant increment was observed. As a result of drug resistant the populations of resistant to first line of treatment and recovered both rise as seen in figure (4.5) and figure (4.6). Figure (4.7) shows the effects of drug resistance on the transmission dynamics of Tuberculosis. In figure (4.7a) to figure (4.7c), we varied the drug resistance rate  $\sigma$  from 0.00 to 0.70. It is observed that exposed and infected classes decreases with an increase in the drug resistance rate while the recovered class increases with increase in drug resistance rate. This is as a result of the second line of treatment introduced. Figure (4.8) shows the

effects of loss of passive immunity rate on the transmission dynamics of Tuberculosis. In figure (4.8a) to figure (4.8c), we varied the loss of passive immunity rate  $\eta$  from 0.00 to 0.45. It is observed that the exposed, infected and recovered classes increases with an increase in the loss of passive immunity rate.

**4. CONCLUSION**

This paper consider passive immunity and resistance to the first line of treatment classes in the existing SEIRS model of tuberculosis. The local stability of the disease free equilibrium point (DFE) was carried out using the method of next generation matrix and the result shows that the disease free equilibrium (DFE) point is locally asymptotically stable (LAS) whenever  $R_0 < 1$  and unstable otherwise. Furthermore the global stability of the disease free equilibrium (DFE) was analyzed using Lasalle-Lyapunov function and the result revealed that the (DFE) is globally asymptotically stable (GAS) whenever  $R_0 \leq 1$ . The numerical results shows the effects of drug resistance and passive immune infant on transmission dynamics of Tuberculosis. Thus, we conclude that, efficacy of drugs ought to be improved and second line of treatment should be enforce in order to control Tuberculosis.

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