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Modeling the Dynamics of Tuberculosis in a Coupled Metapopulation

Mutai Wesley[1], Kirui Wesley[2] and Mukuna Wilys[1]*

[1]*Department of Mathematics and Computer Science, University of Kabianga, Kenya*

[2]*Department of Mathematics and Actuarial Science, South Eastern Kenya University, Kenya*

Abstract

Tuberculosis (TB) is currently one of the key health tests in many developing countries, Kenya included. TB is a curable transmissible ailment caused by *Mycobacterium tuberculosis*. The formation of the tubercles in tissues of the body like in the lung tissues describes the disease. Interaction with transmissible individuals can make one acquire TB. The behavior of transmissible diseases, its impacts and possible future prediction about its spread has been best understood with the knowledge of mathematical epidemiology. In this study, delay differential equations were formulated for purposes of determining stability of Disease Free Equilibrium (DFE). The delay component was incorporated into Susceptible-Exposed-Infectious-Recovered (SEIR) model. A parameter called the basic reproduction number was computed and numerical simulations were done using MATLAB for validation of the analytical results. Parameter values were obtained from secondary data.

Keywords: TB; Reproduction number; Delay differential equations; Stability; Disease free equilibrium

Introduction

Tuberculosis (TB) is a bacterial infections ailment of humans and animals initiated by the *Mycobacterium Tuberculosis Complex* (MTBC) which include four TB causing Mycobacteria*: M. bovis, M. africanum, M .canetti* and *M .microti.* The formation of tubercles on the lungs and other tissues of the body characterize the ailment, frequently developing extensively after the primary infection. It is an airborne disease which is transmitted when individuals with active TB cough, sneeze, speak, sing or spit. *Mycobacterium tuberculosis* is among the causes of mortality [1-17]. In the case of incomplete treatment, the remains of *mycobacterium tuberculosis* in the human system often results in the bacterium developing resistance to antibiotics. This leads to Multi-Drug Resistance-TB (MDR-TB) [9,18].

Mathematical epidemiology has contributed to a more in-depth appreciative of the activities of tuberculosis as a transmissible ailment, its effects and possible future forecast about its spread and the mechanisms of its control. The planning, evaluation, prevention and control of TB in a population will be facilitated by model analysis [11]. Many populations are structured in space but interconnected by human travelling. A population may be subdivided into separated patches also called subpopulations, each with its dynamics. A group of such a distinctive subpopulation is known as a metapopulation [12]. Subpopulation interconnections may be; random, all-to-all, one-to-many or nearest neighbor connection [2].

Coupling configurations

Coupling is the arrangement of subpopulations in a way that can affect each other. There are different forms of nearest neighbor coupling. Nearest neighbor coupling is where a subpopulation is connected to their immediate neighbor [3]. The following are the coupling configurations: Coupling on a line, Coupling on a ring, Coupling on a two-dimensional Bravais lattice, One-to-all coupling, All-to-all coupling and Coupling on three-dimension.

Review of Related Literature

The increasing rate of Tuberculosis (TB) cases in many countries of Sub-Saharan Africa over the past decade is largely attributed to the Human Immunodeficiency Virus (HIV) and other emerging infections. Mathematical models developed for tuberculosis transmission are numerous; some of

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Correspondence:
Mutai Wesley, Department of Mathematics and Computer Science, University of Kabianga, Kericho, Kenya; E-mail: mutaiwesley13@gmail.com

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them have been reviewed as follows: According to [14] they studied the spread of TB through a two patch epidemiological model. They made an assumption that susceptible individuals can migrate between two patches but not infective individuals. They formulated the model by considering a two patch SEI TB. They then analyzed the model by computing the DFE and R_0. They went further and determined the global stability of DFE by showing that DFE has global asymptotic stability when R_0<1. In [5] they formulated a model on pulmonary and MDR TB with vaccination. Here, they considered a quarantine class in their epidemic model for MDR TB patients. They observed that quarantine plays an important part in the control of the infection. They formulated Susceptible-Exposed-Infectious-Quarantine-Recovered-Susceptible having a Vaccinated class (SEI-QRS-V). The model was used in describing changing aspects of TB spread in relation to time in human being populace. The results showed that the disease R_0, DFE and their stability were determined. They showed that if R_0<1, DFE stability is global in the feasible zone and the disease is wiped out. If R_0>1, an exceptional endemic balance occurs and has a nearby (local) asymptotic stability. According to [4] they studied a non-linear mathematical model of TB with a case detection and treatment. In the paper, the whole population under consideration was in four compartments; Susceptible Exposed Infectious and Recovered (SEIR) model which they used to study transmission dynamics of TB. They computed R_0 and determined the equilibria of the model. Their results showed that an increase in the rate of case detection lead to an increase in the threshold value of R_0. Also, the treatment reduced the equilibrium level of the infective class.

According to [13] they presented a paper titled 'mathematical model for vaccinated tuberculosis disease with VEIT model'. In this model, there are four compartments; Vaccinated Exposed Infected and Treated (VEIT). The paper discussed about formation and analysis of the VEIT model to TB virus infection by exogenous re-infection. They concluded that the model of vaccinated with exogenous re-infection have two equilibria states; DFE and EEP. They showed that the eigenvalue of DFE is always negative so that the system stability is asymptotically stable at DFE.

In [6] a mathematical model that predicted the threat of TB as a contagious airborne infection under stable state and non-unstable state situations was developed. They did this by monitoring the amount of breath out air by contagious persons in a restricted environment. They demonstrated precisely and diagrammatically, the relationship between TB spread possibility and airborne level of infection, average amount of exhaled air taking into consideration TB occurrence and length of contact to contagious persons in a restricted environment. They chose an age structuring model since infection and illness frequency differ in diverse inhabitants on age dependent and host immune aspects. In their study, they found out that TB spread is prevalent in gatherings for instance; schools, public transportation and correctional facilities especially in developing countries. Similarly [1] in his thesis titled 'mathematical modeling of population dynamics of TB' presented and analyzed a SLIT (Susceptible Latent Infectious and Treated) model with the inflow of infective. He analyzed the spread, asymptotic behavior and possible eradication of the disease. He also carried out sensitivity analysis of R_0 to determine the parameter value that contributes more on the disease transmission. He utilized the sensitivity index analysis using partial derivatives when the variable is a differentiable function of the parameter. With the help of next generation matrix and theorem by [15], it was found out that whenever R_0>1, DFE is locally asymptotically stable and unstable whenever R_0>1. The simulation results from the thesis indicated that despite presence of constant inflow of infective immigrants, he proposed a control strategy of complete treatment that can help suppress the spread of TB. According to [16] a compartmental model to describe the population dynamics of TB disease in a prison system in South Africa was developed. Their model considered the inflow of susceptible and exposed classes as well as the disease infection into the prison population. The model was used to make quantitative projections of TB prevalence and measure on effects of interventions. In their paper, they presented a deterministic compartmental model using ODE's and determined the global stability of disease Free State a parameter for eradicating TB. In [8] they modeled the effect of combining Immunization with Latent Tuberculosis treatment in controlling the spread of Tuberculosis. The administration of Bacillus Calmette Guerin (BCG) vaccines at birth protects children from early infection of the disease, but the effect of these vaccines expires with time. Their results showed that detection and treatment of latent tuberculosis infections using Isoniazid Preventive Therapy prevents the breakdown of latent infections into infectious cases, thus reducing greatly the rate of spread of the disease since only members of the infectious class can spread the disease to others. The DFE will be stable if effort is intensified in bringing down both the contraction rate and the rate of break down to infectious tuberculosis. According to [7] they developed a mathematical model of the spread of TB disease involving the age classes in a susceptible compartment under SEIR model. The model had two equilibrium points; DFE and EEP. The R_0 was constructed using the next generation matrix approach. They found out that TB transmission can be reduced through vaccination and increasing life expectancy. The results from simulation showed also that transmission can also be reduced through vaccine protection period and vaccine efficacy. The above studies did not consider the use of Delay Differential Equations (DDE) in the solution to the various equations arising from the models. This study has formulated DDE`s model for the spread of TB in a coupled metapopulation.

Methodology

Introduction

In epidemiology, the basic reproductive number (sometimes basic reproduction rate or ratio) of an infection is the number of cases one case generates on the average over the course of its infectious period. This metric is useful because it helps determine whether or not an infectious disease can spread through a population. The basic Reproduction number R_0 is the threshold for many epidemiological models. When R_0<1, the infection dies out in the long run (i.e. each infected individual produces one average less than one new infected individual). One the other hand, if R_0>1 the infection will be able to spread in a population (i.e. each infected individual produces more than one new infected individual).

To obtain R_0, the dominant eigenvalue of the next generation matrix is considered such that $R_0=\rho(FV^{-1})$ where ρ is the spectral radius of next generation matrix, Matrix F_i represents the rate of new infection entering compartment i and matrix V_i represents the rate of transfer into and out of compartment i by other ways.

Since we are dealing with a large population, a deterministic or compartmental mathematical model is used. In the deterministic model, individuals in the population are assigned to different subgroups or compartments, each representing a specific stage of the epidemic. The Susceptible-Exposed-Infected Removed (SEIR) epidemiological models are utilized to study and analyze the disease, thus the simple SEIR model is used to explain the spread of tuberculosis in a population.

Methods of solution

The stability of the model has been approached from Jacobian matrix method for checking stability of Disease Free Equilibrium (DFE) and numerical simulations have been done using MATLAB to validate the analytic results.

Model equations

The dynamics of TB is modeled by the following system of delay differential equations:

$$\frac{ds_i}{dt} = A_i - \mu_i s_i - \beta_{ij}\sum_{j=i-1}^{i+1} S_i I_j(t-\tau) - \beta_{ii} S_i I_i(t-\tau) \quad (3.1)$$

$$\frac{ds_j}{dt} = A_j - \mu_j sj - \beta_{ij}\sum_{i=j-1}^{j+1} S_j I_i(t-\tau) - \beta_{jj} S_j I_j(t-\tau) \quad (3.2)$$

$$\frac{dE_i}{dt} = \beta_{ij}\sum_{j=i-1}^{i+1} S_i I_j(t-\tau) - (1-\varepsilon_i)E_i(t-\tau) - E_i(\mu_i + d_i)\beta_{ii} S_i I_i(t-\tau) \quad (3.3)$$

$$\frac{dE_j}{dt} = \beta_{ji}\sum_{i=j-1}^{j+1} S_j I_i(t-\tau) + (1-\varepsilon_j)E_j(t-\tau) - E_j(\mu_j + d_j)\beta_{jj} S_j I_j(t-\tau) \quad (3.4)$$

$$\frac{dI_i}{dt} = \varepsilon_i E_i(t-\tau) + (1-\gamma_i)I_i(t-\tau) - I_i(\mu_i + d_i) \quad (3.5)$$

$$\frac{dI_j}{dt} = \varepsilon_j E_j(t-\tau) + (1-\gamma_j)I_j(t-\tau) - I_j(\mu_j + d_j) \quad (3.6)$$

$$\frac{dR_i}{dt} = \gamma_i I_i(t-\tau) - \mu_i R_i - \sigma R_i \quad (3.7)$$

$$\frac{dR_j}{dt} = \gamma_j I_j(t-\tau) - \mu_j R_j - \sigma R_j \quad (3.8)$$

Model preliminary analysis

Positivity and boundedness of solutions: Since the model under consideration represents the population dynamics of living organisms, it is necessary to show that the solutions are always positive and bounded.

We define the compact set

$\{S_i(0), E_i(0), I_i(0), R_i(0)\}\varepsilon\mathbb{R}^4 \geq 0$, $0 \leq E_i < S_2$, $0 \leq I_i < S_2$, $0 \leq R_i < S_3$ where $S_a > 0, a = 1,2,3.$

Proposition 1: The set Ω is positively invariant for model (3.2), (3.4), (3.6) and (3.8).

Proof:

We have $\frac{dS_i}{dt} | S_{i=0} = \Lambda_i \geq 0$ (3.10)

$\frac{dE_i}{dt} | E_{i=0} = 0 = \beta_{ij}\sum_{j=i-1}^{i+1} S_i I_j(t-\tau) - \beta_{ii} S_i I_i(t-\tau) \geq 0$ Whenever $S_i, I_j, I_i \geq 0$ (3.11)

$\frac{dI_i}{dt} | I_{i=0} = 0 = \varepsilon_i E_i(t-\tau) \geq 0$ whenever $E_i \geq 0$ (3.12)

$\frac{dR_i}{dt} | R_{i=0} = 0 = \gamma_i I_i(t-\tau) \geq 0$ (3.13)

This confirms that $\{S_i(t), E_i(t), I_i(t), R_i(t)\}\varepsilon\mathbb{R}^4 \geq 0$ with $\{S_i(0), E_i(0), I_i(0), R_i(0)\}\varepsilon\mathbb{R}^4 \geq 0$

Thus $\mathbb{R}^4 \geq 0$ is positively invariant for model (3.2) - (3.8).

For boundedness we define;

$\frac{dS_i}{dt} = \gamma_i\varepsilon_i[\Lambda_i - u_i S_i]$

$\frac{dS_i}{dt} = \gamma_i\varepsilon_i[E_i(u_i + d_i)]$

$\frac{dI_i}{dt} = \gamma_i(1-\varepsilon_i)[I_i(u_i + d_i)]$

$\frac{dR_i}{dt} = -(1-\gamma_i)[u_i - \sigma]R_i]$

Then

$$N(t) = S_i(t) + E_i(t) + I_i(t) + R_i(t)$$

Let c min $(u_i\gamma_i\varepsilon_i\gamma_i\varepsilon_i(u_i + d_i), \gamma_i(1-\varepsilon_i)(u_i + d_i), (1-\gamma_i)(u_i + \sigma)$

Then

$$\frac{dN(t)}{dt} = \Lambda_i\gamma_i\varepsilon_i - c(s_i(t) + E_i(t) + I_i(t) + R_i(t))$$

$$\frac{dN(t)}{dt} \le \omega - N_i(t)$$

Where $\omega = \Lambda_i\gamma_i\varepsilon_i$

$$\frac{dN(t)}{dt} + cN_i(t) \le \omega$$

$$N(t)e^{ct} \le \omega e^{ct} - \omega e^0 + N_0$$

$$N(t) \le \omega + N_0 e^{-ct} - \omega e^{-ct}$$

Where $\omega \ge 0$. This shows that the solution is bounded.

To obtain R_0, the dominant eigenvalue of the next generation matrix is considered such that $R_0=\rho(FV^{-1})$ where ρ is the spectral radius of next generation matrix, Matrix F_i represents the rate of new infection entering compartment *i* and matrix V_i represents the rate of transfer into and out of compartment *i* by other ways.

From the equations (3.1)-(3.8) the matrices $\boldsymbol{F_i}$ and V_i are given by;

$$F_i = \begin{pmatrix} (1-\varepsilon_i)E_i(t-\tau) \\ (1-\varepsilon_j)E_j(t-\tau) \\ (1-\gamma_i)I_i(t-\tau) \\ (1-\gamma_j)I_j(t-\tau) \end{pmatrix} \tag{3.18}$$

$$V_i = \begin{pmatrix} E_i(\mu_i + d_i) \\ E_j(\mu_j + d_j) \\ I_i(\mu_i + d_i) \\ I_j(\mu_j + d_j) \end{pmatrix} \tag{3.19}$$

We then differentiate matrix F_i and V_i partially with respect to state variables to obtain the below 4 × 4 matrices as;

$$F_i = \begin{bmatrix} (1-\varepsilon_i)e^{-\lambda\tau} & 0 & 0 & 0 \\ 0 & (1-\varepsilon_j)e^{-\lambda\tau} & 0 & 0 \\ 0 & 0 & (1-\gamma_i)e^{-\lambda\tau} & 0 \\ 0 & 0 & 0 & (1-\gamma_j)e^{-\lambda\tau} \end{bmatrix} \tag{3.20}$$

$$V_i = \begin{bmatrix} \mu_i + d_i & 0 & 0 & 0 \\ 0 & \mu_j + d_j & 0 & 0 \\ 0 & 0 & \mu_i + d_i & 0 \\ 0 & 0 & 0 & \mu_j + d_j \end{bmatrix} \tag{3.21}$$

Then, the inverse of V is given by;

$$V^{-1} = \begin{bmatrix} \frac{1}{\mu_i + d_i} & 0 & 0 & 0 \\ 0 & \frac{1}{\mu_j + d_j} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_i + d_i} & 0 \\ 0 & 0 & 0 & \frac{1}{\mu_j + d_j} \end{bmatrix} \tag{3.22}$$

The next generation matrix FV^{-1} is given by;

$$FV^{-1}=\begin{bmatrix}(1-\varepsilon_i)e^{-\lambda\tau} & 0 & 0 & 0\\ 0 & (1-\varepsilon_j)e^{-\lambda\tau} & 0 & 0\\ 0 & 0 & (1-\gamma_i)e^{-\lambda\tau} & 0\\ 0 & 0 & 0 & (1-\gamma_j)e^{-\lambda\tau}\end{bmatrix}\begin{bmatrix}\frac{1}{\mu_i+d_i} & 0 & 0 & 0\\ 0 & \frac{1}{\mu_j+d_j} & 0 & 0\\ 0 & 0 & \frac{1}{\mu_i+d_i} & 0\\ 0 & 0 & 0 & \frac{1}{\mu_j+d_j}\end{bmatrix} \tag{3.23}$$

Which simplifies to;

$$FV^{-1}=\begin{bmatrix}\frac{(1-\varepsilon_i)e^{-\lambda\tau}}{\mu_i+d_i} & 0 & 0 & 0\\ 0 & \frac{(1-\varepsilon_j)e^{-\lambda\tau}}{\mu_j+d_j} & 0 & 0\\ 0 & 0 & \frac{(1-\gamma_i)e^{-\lambda\tau}}{\mu_i+d_i} & 0\\ 0 & 0 & 0 & \frac{(1-\gamma_j)e^{-\lambda\tau}}{\mu_j+d_j}\end{bmatrix} \tag{3.24}$$

The eigenvalues of the matrix (3.24) are computed by $|A-I\lambda|=0$ given where A is the matrix FV^{-1} and i is 4×4 identity matrix.

$$\lambda_1=\frac{(1-\varepsilon_i)e^{-\lambda\tau}}{\mu_i+d_i}$$

$$\lambda_2=\frac{(1-\varepsilon_j)e^{-\lambda\tau}}{\mu_j+d_j}$$

$\lambda_{3,4}$ is obtained from the characteristic equation below;

$$\lambda^2-\lambda\left(\left(\frac{(1-\gamma_i)e^{-\lambda\tau}}{\mu_i+d_i}\right)+\left(\frac{(1-\gamma_j)e^{-\lambda\tau}}{\mu_j+d_j}\right)\right)+\left(\left(\frac{(1-\gamma_i)e^{-\lambda\tau}}{\mu_i+d_i}\right)+\left(\frac{(1-\gamma_j)e^{-\lambda\tau}}{\mu_j+d_j}\right)\right)=0$$

Algebraically,

$$\lambda_3=\frac{(1-\gamma_j)e^{-\lambda\tau}}{\mu_j+d_j}$$

$$\lambda_4=\frac{(1-\gamma_i)e^{-\lambda\tau}}{\mu_i+d_i}$$

Thus R_0 which is given by the dominant eigenvalue is given as;

$$R_0=\frac{(1-\gamma_i)e^{-\lambda\tau}}{\mu_i+d_i}$$

Equilibrium points and stability analysis

In epidemiology, there are basically two equilibrium points, namely Disease Free Equilibrium (DFE) where *i=0* and Endemic Equilibrium Point (EEP) where $i \neq 0$. DFE occurs in absence of disease while EEP occurs in presence of a disease. The stability of a system is locally studied near fixed points. A system is stable if all the eigenvalues of the system linearized about a fixed point have negative real parts. This condition for stability yields a reproductive ratio denoted by R_0 which will form a stability criterion.

Disease free equilibrium: This equilibrium point describes a point when the rate of change is equal to zero. It is evaluated by equating the system of delay differential equation (3.1)-(3.8) to zero. DFE occurs when the infective class is absent and consequently the recoveries.

Stability of Disease Free Equilibrium: The disease free equilibrium is the state of variable of the model in the absence of disease. Its stability can be tested using the eigenvalues of the Jacobian matrix obtained at DFE, where at this point $R_0<1$. To obtain Jacobian matrix we differentiate

equations (3.1)-(3.8) with respect to state variables at DFE to get.

$$FV^{-1}=\begin{bmatrix} -\mu_i & 0 & 0 & 0 & -\beta_{ii}s_i e^{-\lambda\tau} & \beta_{ij}\sum_{i=j-1}^{j+1} s_j e^{-\lambda\tau} & 0 & 0 \\ 0 & -\mu_j & 0 & 0 & -\beta_{ij}\sum_{i=j-1}^{j+1} s_j e^{-\lambda\tau} & -\beta_{ii}s_i e^{-\lambda\tau} & 0 & 0 \\ 0 & 0 & (1-\varepsilon_i e^{-\lambda\tau})-(\mu_i+d_i) & 0 & \beta_{jj}s_j e^{-\lambda\tau} & \beta_{ij}\sum_{j=i-1}^{i+1} s_i e^{-\lambda\tau} & 0 & 0 \\ 0 & 0 & 0 & (1-\varepsilon_j e^{-\lambda\tau})-(\mu_j+d_j) & \beta_{ij}\sum_{i=j-1}^{j+1} s_j e^{-\lambda\tau} & \beta_{jj}s_j e^{-\lambda\tau} & 0 & 0 \\ 0 & 0 & \varepsilon_i e^{-\lambda\tau} & 0 & (1-\gamma_i)e^{-\lambda\tau}-(\mu_i+d_i) & 0 & 0 & 0 \\ 0 & 0 & 0 & \varepsilon_j e^{-\lambda\tau} & 0 & (1-\gamma_j)e^{-\lambda\tau}-(\mu_j+d_j) & 0 & 0 \\ 0 & 0 & 0 & 0 & (1-\gamma_i)e^{-\lambda\tau} & 0 & -\mu_i & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\mu_j \end{bmatrix} \quad (3.25)$$

The system (3.1)-(3.8) is locally asymptotically stable if all the eigenvalues of linearization matrix (3.25) above are negative. The eigenvalues are:

$$\lambda_1=-\mu_i$$

$$\lambda_2=-\mu_j$$

$$\lambda_3=-\mu_i$$

$$\lambda_4=-\mu_j$$

$$\lambda_5=(1-\varepsilon_i)e^{-\lambda\tau}-(\mu_i+d_i)$$

$$\lambda_6=(1-\varepsilon_i)e^{-\lambda\tau}-(\mu_j+d_j)$$

$$\lambda_{7,8}==-(1-\gamma_i)e^{-\tau\lambda}-(\mu_j+d_j)-(1-\gamma_j)e^{-\tau\lambda}-(\mu_j+d_j))\pm\sqrt{-(1-\gamma_i)e^{-\tau\lambda}+(\mu_j+d_j)(1-\gamma_j)e^{-\tau\lambda}-(\mu_j+d_j))^2-4(-(1-\gamma_i)e^{-\tau\lambda}+)(\mu_j+d_j)(1-\gamma_j)e^{-\tau}}$$

Which simplifies to

$$\gamma je^{-t\lambda}-(\mu_j+d_j)<0$$

$$\gamma je^{-t\lambda}<(\mu_j+d_j)$$

$$\frac{\gamma ie^{-\lambda\tau}}{\mu j+dj}<1$$

Thus $R_0=\frac{\gamma ie^{-\lambda\tau}}{\mu j+dj}<1$

When R_0<1, DFE is attained.

Numerical Analysis and Results

This chapter comprises of parameter values obtained from secondary data and graphs obtained using Mat lab (Table 1).

Table 1: Parameters, Definition and Value.

Parameters	Definition	Value
μ	Natural death rate coefficient	0.5
d	Disease-induced death rate	0.2
β	Probability that susceptible becomes infected	0.001
γ	Treatment rate	$0 \le \gamma \le 1$
ε	Rate at which exposed individuals become infectious	0.5
Λ	Recruitment rate	0.005
S_0	Initial susceptible population	1000
I_0	Initial infected population	50
R_0	Initial recovered population	15
N_0	Initial population	1165
E_0	Initial exposed population	100
τ	Time delay	To be determined

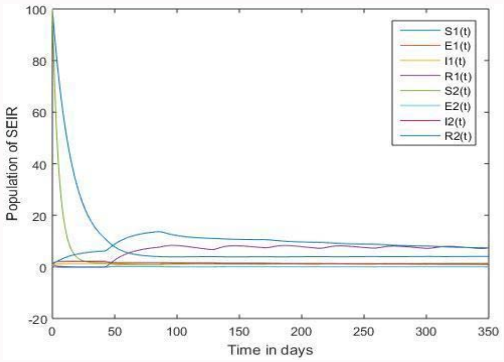

Figure 1: Population of various compartments against time in days. From the graph, it is evident that, initially the infected were at 80, then it drops drastically to below 20 because treatment, time delay and vaccination played a major role in minimizing infection.

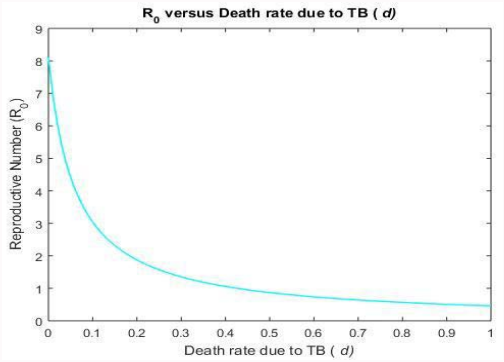

Figure 2: Reproduction number against death rate (d). From the graph it is evident that R_0 is inversely proportional to d.

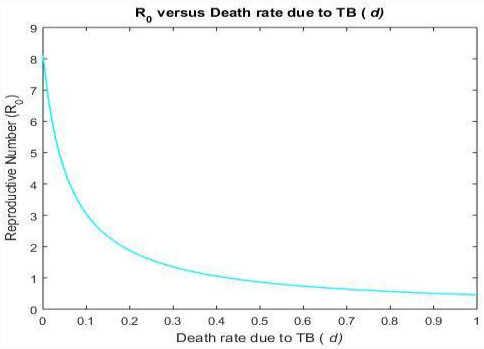

Figure 3: R_0 against progression rate. Form the graph it is evident that R_0 is inversely proportional to progression rate.

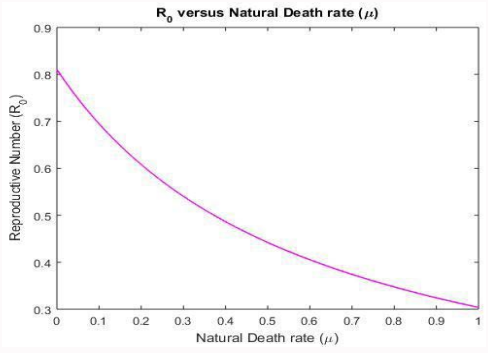

Figure 4: R_0 death rate. From the graph it is evident that R_0 is inversely proportional to death rate, μ.

Conclusion

We have formulated a delay differential equation of SEIR TB model in a coupled Meta population. We obtained a basic reproduction number R_0 which is less than unity. This ratio plays a vital role in minimizing the spread of tuberculosis (Figures 1-4). The spread of contagious diseases remains a test in developing countries. The government should increase educational awareness on restriction of travel of people in and out of a subpopulation to avoid the infection. This will minimize the spread of the disease across the sub-populations. To lower transmission and spread of the disease in a metapopulation, there is need to use of preventive measures such as isolation of already infected individuals, campaigns on BCG vaccination of all children under 5 years and seeking medical treatment on infected persons.

Suggestions for Further Research

This study has not exhausted all about TB dynamics in coupled Metapopulation. The effect of an individual's immune response to TB disease is not included. The model can be extended to include co-infection between TB and HIV in a metapopulation. The carrying capacity of the subpopulation, characteristics of the subpopulations like education levels and economic status are also possible insights for further research work on the dynamics of TB disease in Meta-populations.

References

1. Adebiyi AO. Mathematical modeling of population dynamics of tuberculosis, unpublished Master's Thesis University of the Western Cape. 2016.
2. Adu AMW, Rotich KT. Synchronization, persistence in diffusively coupled lattice oscillators, Sultan Qaboos University. J Sci. 2007;12(1):41-52.
3. Anupi OP. Modeling the dynamics of an epidemic in a metapopulation lattice, unpublished Master's Thesis. 2015.
4. Athithan S, Ghosh M. Optimal control of tuberculosis with case detection and treatment. J Model Simulat. 2015;11(2):111-22.
5. Bimal KM, Jyotika S. Mathematical model on pulmonary and multidrug-resistant tuberculosis patients with vaccination. J Egypt Mathemat Society. 2013;22(2):311-6.
6. Chacha M. Issarow. Modeling the transmission of tuberculosis, unpublished Master's thesis, University of Cape Town. 2016.
7. Dipo A, Riyanto ZA, Bustamam A. A mathematical model of TB control with vaccination in an age-structured susceptible population. J physi Conf Serie. 2018;1108.
8. Enagi AI, Ibrahim MO, Akinwande NI, Bawa M, Wachin AA. A Mathematical model of tuberculosis control incorporating vaccination, latency and infectious treatments (case study of Nigeria). Int J Mathemat Computer Sci. 2017;12(2):97-106.
9. Fonseca KL, Rodrigues PNS, Olsson IA, Saraiva M. Experimental study of tuberculosis: from animal models to complex cell systems and organoids. PLOS Pathog. 2017;13(8):e10006421.
10. Global Tuberculosis Report. 2013.
11. Herthcote HW. The mathematics of infectious diseases. J Society Industrial Applied Mathemat. 2000;42(4):599-653.
12. Jesse M, Ezano P, Davis S, Hesterbeek J. A fully coupled mechanistic model for infectious disease dynamics in a metapopulation movement and epidemic duration. J Theor Biol. 2008;254(2):331-5.
13. Muhammad RT, Lestari D, Septiarini TW. Mathematical model for vaccinated Tuberculosis disease with VEIT model. Int J Model Optimizat. 2015;5(3):192-7.
14. Tewa JJ, Bowong S, Mewoli B. Mathematical analysis of two-patch model for the dynamical transmission of tuberculosis. J Appl Mathemat Model. 2012;36:2466-85.
15. Van den Driesch, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. J Mathemat Biosci. 2002;180(1):29-48.
16. Witbooi P, Vyabwera SM. A model of population dynamics of TB in a prison system and application to South Africa. BMC Res Notes. 2017;10(1):643-97.
17. Wu P, Lau EHY, Cowling BJ, Chi-Chiu L, Cheuk-Ming T, Leung GM. The transmission dynamics of tuberculosis in a recently developed Chinese city. PLOS ONE. 2010;5(5):e10468.
18. Zhao Y, Li M, Yuan S. Analysis of transmission and control of Tuberculosis in mainland China, 2005-2016, based on the age-structure mathematical model. Int J Environ Res Public health. 2017;14(10):1192.