ABSTRACT

In this project, a deterministic mathematical model of tuberculosis incorporating case detection and drug resistance with constant recruitment rate was developed. The population was subdivided into six compartments according to their disease status. The basic reproduction number of the model was obtained using the next generation matrix. The disease free and endemics equilibrium points was derived and it was proved that the disease endemic equilibrium state exist if $R_0 > 1$. The results show that the disease free equilibrium points are locally asymptotically stable if $R_0 < 1$ and globally stable if $R_0 \leq 1$. Also the results further show that The endemic equilibrium points are locally asymptotically stable if $R_0 > 1$ and globally stable if $R_0 \geq 1$.We obtain the approximate solution of the model using Homotopy Perturbation Methods. The graphical summaries of the solution were carried out and the result show that increase in case detection and sustained treatment can help to reduce transmission of tuberculosis disease.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background to the Study

Tuberculosis is a bacterial disease which attacks some part of the human body such as lungs, bones, lymph nodes and brain. This disease is caused by a known mycobacterium tuberculosis that looks like rod-shape bacterium. Some of the symptoms are in the form of cough, chest pains, shortness of breath, loss of appetite, weight loss, fever, chills and fatigue.

Tuberculosis is the second leading cause of death from infectious disease worldwide after those caused by Human Immune Deficiency Virus (HIV) (Daniel 2006). This disease affect over 2 billion of the world population. Approximately over nine million people develop active tuberculosis and up to 2 million death cases is recorded from tuberculosis every year. Also

over 480 thousand people developed drug resistance to tuberculosis with 210 thousand of those who developed multi drug resistance tuberculosis result to death. (Klein *et al*. 2007).

Tuberculosis mostly affect adults in their most productive years, however people of ages are at risk of having active tuberculosis. Over 95% of all tuberculosis cases and deaths are in developed countries. HIV infected people are 20 to 30 times likely to developed active tuberculosis than others, the risk of active tuberculosis is also higher in persons suffering from other conditions that weaken the immune system of the body.

According WHO report over 1 million children that fall within the age bracket of 0-14 years are being diagnosed with Tuberculosis disease, and 230,000 children (including children with associated HIV tuberculosis) died from the disease in 2017. Also those who smoke are at high risk of having tuberculosis disease and higher death rate. With over 79% of tuberculosis cases worldwide are attributed to smoking alone (WHO report 2018).

Tuberculosis (TB) infection is of two type, namely, latent infection and active infection. The latent infection in the body system is a condition in which a patient holds dormant (sleeping) Tuberculosis bacteria in the body and they do not cause TB disease to the patient's body. However, in a certain period, the sleeping bacteria would be awake and become active. People infected latently are called latent TB patients and are unable to infect those vulnerable to TB disease. Actively infected is a state in which the bacteria causing tuberculosis in the patient's body are actively multiplying and the disease symptoms becomes very visible in the body system. Those patients that are infected actively are called active tuberculosis and they can transmit the disease to vulnerable people (Lisa *et al*., 2009).

Patients of latent and active TB can be treated but they are not totally protected from the disease. Within a certain time, those who recovered can be re-infected again in case contact with TB infectious patient. Based upon the chain of actions of TB bacteria infection, the associated population can be grouped into several different sub-populations which are susceptible to the TB disease. The sub-population groups are latent infectious, active infectious and recovered infectious groups (Lisa *et al*., 2009).

Tuberculosis is curable and treatable this disease however total elimination may not be possible because of difficulty in developing an effective vaccine for the disease (WHO report, 2011). Transmission of tuberculosis can be controlled by providing proper medical treatment to people infected with the disease. In many cases a lot of people that are infected with tuberculosis don't know their status and they may transmit this disease to others. Sometimes infected individuals may stop receiving treatment and this also could result in new tuberculosis infection to people around them (Arthitian *et al.*, 2013).

According to Semenza *et al.* (2010) over the last twenty 25 years the disease death rate has significantly drop to 45% due to early detection and proper diagnosis and treatment. However the world is still far from overcoming the disease. Thus mathematical modelling will be of valuable importance if the 2030 target of sustainable development goal of ending tuberculosis is to be achieved (WHO report, 2018).

1.2 Statement of the problem

Tuberculosis has becomes one of the greatest death threat globally. According to World Health Organization (WHO) report in 2017 an estimated ten million people fell ill with 1.6

million death record from the disease. This research seek to investigate the effects of case detection and resistance in controlling the transmission and spread of tuberculosis disease.

1.3 Significance of the Study

The study on modelling the effects of case detection and resistance to tuberculosis disease will be very helpful in the sense that, what people normally did not attribute importance to can be periscope using mathematical tool.

1.4 Justification of the Study

Medical workers and health Authorities have devoted substantial effort and resources into trying to predict and control the spread of tuberculosis disease. It is hoped therefore that the result of this study will serve as control and preventive measure in the following ways.

i. The result of the study will help health workers or practitioners the importance of early case detection in reducing the spread of tuberculosis diseases.
ii. It will serve as bases for future research in mathematical modelling of tuberculosis diseases.
iii. The result of the study will also help medical workers on how case detection could affect drug resistance.

1.5 Scope and Limitation of the Study

This research focus only on effects of case detection incorporating resistance class. The research do not consider the vaccinated fraction of the susceptible population and immunity level of an individuals.

1.6 Aim and Objective of the Study

The aim of this research is to develop and analyse a mathematical models on effects of case detection and resistance to the spread of tuberculosis disease.

The specific objectives are to:

i. Formulate a mathematical model on tuberculosis incorporating resistance classes and case detection parameter.
ii. Obtain the invariant region of the model.
iii. Obtain the positivity of the solutions.
iv. Obtain the equilibrium of the model.
v. Compute the basics reproduction number R_0 using next generation matrix.
vi. Discuss the stability of both disease free and endemic equilibrium points in respect to basic reproduction number R_0.
vii. Solve the model via homotopy perturbation method.

1.7 Definition of terms

i. **Mathematical Modelling:** is an abstract model that uses mathematical language to describe the relationship and behaviour of the system.

ii. **Case Detection Rate of TB:** is the ratio of the number of notified tuberculosis cases to the number of incident tuberculosis cases in a given year.

iii. **Resistance Classes:** refer to the class of people that is resistant to tuberculosis treatment.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Overview of Tuberculosis Diseases with Treatment and Resistant to Multi-Drug Resistance (MDR)

Tuberculosis is an airborne disease caused by bacteria (mycobacterium tuberculosis). Tuberculosis occur in all part of the world with common symptoms of active lungs such as cough, with sputum and blood at times, chest pains, weakness and weight loss, fever and night sweats. Today this disease rank the second most common cause of death worldwide after those due to HIV/AIDS. In 2017 over ten million people fell ill with tuberculosis disease and 1.6 million death were recorded with 62% of this cases happen in the south east Asia and western pacific regions followed by the African regions which account for 25% of tuberculosis new cases, 87% of this new cases occur in the 30 high burden countries and eight countries accounted for two-third of the total cases in 2017 which are India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh and south Africa (WHO Report 2018).

Tuberculosis disease can be classified into two stages which are latent and active tuberculosis. A person with latent tuberculosis infection has tuberculosis bacteria in his body but the bacteria are inactive, does not fall sick, is not contagious and has the potential to developed disease if the bacteria become active and multiply in his body, though the disease is treatable which means that progression to infectious class of individuals can be prevented. Similarly, a person with active Tuberculosis disease feel sick and experience symptoms such as coughing, fever and weight loss. The person is capable of spreading the disease to other if the

tuberculosis bacteria are active in the lung or throat and is curable provided an early diagnosis and treatment is administered to the patient (Heartland National Tuberculosis Centre, 2006)

About one-third of the world population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease. People infected with TB bacteria have a 10 % lifetime risk of falling ill with Tuberculosis disease. Latent Tuberculosis infection can progress to active tuberculosis when the immunity of the host decreases due to aging, stress, over use of immunosuppressant or co-infection with HIV (WHO Report, 2018).

Tuberculosis is a treatable and curable disease. Active drug-susceptible tuberculosis disease is treated with a standard six month course of four antimicrobial drugs that are provided with full supervision and support to the patients by a health workers or trained volunteer to ensure that the patients adhere to their treatment prescriptions properly. 54 million lives were saved through diagnosis and treatment between 2000 to 2017 (WHO Report 2018).

Treatment failure can lead to drug resistance which is a challenge to control programs as these drug resistant strains are more difficult to treat (Blower et al. 1996). According to World Health Organization (WHO) multi-drug resistant tuberculosis (MDR-TB) remains a public health crises and health security threat. In 2017 it was estimated that 558000 new cases with resistance to rifampicin the most effective first line drug treatment of which 82% had MDR-TB. Globally TB incidence is falling at about 2% per year, this need to accelerate to 4-5%annual decline to reach the 2030 milestone of ending tuberculosis (WHO Report 2018).

2.2 Overview of Tuberculosis Modelling

Over the past 10 years they have being a significant improvement in tuberculosis (TB) research, mostly in areas of diagnostic test development an treatment routines for TB and multidrug resistant TB (MDR-TB) McNerney *et al.* (2012).

The spread of tuberculosis diseases can be analysed through mathematical models. The model can help to predict and control the spread of tuberculosis outbreak in the future. The spread of tuberculosis disease can be modelled with some types of epidemics modelled including the models of SIR (Susceptible, Infected, and Recovered) with or without delay (Taufiq *et al*. 2017).

Waaler and Anderson (1962) developed the first tuberculosis model for the transmission dynamics of tuberculosis since then over 400 paper work have being submitted on tuberculosis modelling .

Okuonghae (2013) developed a mathematical model that incorporate genetics heterogeneity into tuberculosis epidemics. His results show that if a larger of susceptible individuals that have no or partials resistance to tuberculosis get infected and move into the class of normal progressions then even in the worst case scenario of having a huge transmission rate, the disease can still be managed with effective and comprehensive treatment and little incidence of self-cure.

Fredlina et al (2012) build SIR type of mathematical modelling on the spread tuberculosis by considering Multi-drug resistance. They show that the spread of tuberculosis disease can be controlled by reducing the rate of epidemics transmission and increase the recovery rate. They

suggested that in other to reduce the rate of infection of tuberculosis they should reduce the interaction infected individuals and the susceptible populations, whereas to increase recovery rate the sustained medical treatment need to be conducted.

Juan (2010) also developed mathematical model of tuberculosis epidemics by considering the strengths and limitations of using homogeneous mixing and heterogeneous mixing epidemic models to explore the context of the transmission dynamics of tuberculosis. He proved that if the basic reproduction number R_o <1, then the Disease Free Equilibrium is globally asymptotically stable on the nonnegative orthant and if R_o >1an endemic equilibrium exists and is globally asymptotically stable.

Young *et al.* (2008). Studies show that tuberculosis can be cured if an early treatment is made and one follows the proper treatment rule which would normally take six months up to two years for the active tuberculosis to be treated. Sharma et al (2017) show that the infected population is similar on the sociological and -psychological effect rate.

Luju and Yang (2014) developed a mathematical model of tuberculosis incorporating treatment interruption and two latent periods. His result shows that treatment of active tuberculosis cases always help to control tuberculosis epidemics, while treatment interruptions may have negative, positive or no effects on controlling TB epidemics

Athithan *et al*. (2013) developed a nonlinear four compartment(SEIR) mathematical model of tuberculosis with effects of case detection and treatment, his results show that tuberculosis model exhibit backward bifurcation and that increase in case detection rate shift backward bifurcation diagram toward right which leads to an increase in threshold value of reproduction number. He also shows that treatment reduce the equilibrium level of infective populations.

He suggested that an accurate estimation of parameter and the level of control measure are required to reduce the infection prevalence of Tuberculosis in endemic and just $R_0 < 1$ is not enough to eliminate the diseases from the population. His model equation is as follow

$$\frac{dS}{dt} = \Lambda - \mu S - \left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) IS \tag{2.1}$$

$$\frac{dE}{dt} = (1-p)\left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) IS - \beta EI - \left(\mu + v_1 + \vartheta\right) E \tag{2.2}$$

$$\frac{dI}{dt} = p\left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) IS + \beta EI - \left(\mu + \delta_1 + v_2 \eta\right) I + \vartheta E \tag{2.3}$$

$$\frac{dR}{dt} = v_1 E + v_2 \eta I - \mu R \tag{2.4}$$

Where η is case detection rate and v_1, v_2 are treatment parameter for the exposed and infected individuals respectively.

Komsiyah (2013), developed a model on the spread of tuberculosis epidemics in SIR-type by reviewing two different models consisting of vaccination and without vaccination and studied the result generated by the two models. Syahrini *et al* (2017) also developed a mathematical model of SEIR-type by considering the existence of latent group and vaccine administration to the susceptible population. They suggested that vaccination will lower the transmission of tuberculosis disease.

Similarly Nainggolan *et al*. (2013), developed a mathematical modelling on tuberculosis transmission of five compartment (SVEIR) by considering the total number of recovered individual either from natural recovery or due vaccination. He assume that BCG vaccine

moves individuals from the susceptible compartment to the vaccinated populations at the rate ϑ and also peoples that developed immunity to tuberculosis after vaccination moves from vaccinated population to recovered class. His results show that vaccination is capable of reducing the number of latent infectious population. His model equation is as follow

$$\frac{dS}{dt} = \Lambda - \lambda_1 S - (\mu + \vartheta) S \tag{2.5}$$

$$\frac{dV}{dt} = \vartheta S - (1-\sigma)\lambda_1 V - (\mu + r) V \tag{2.6}$$

$$\frac{dE}{dt} = A\lambda_1 S + (1-\sigma)\lambda_1 V - \delta_1 \lambda_1 E - (\mu + k) E + f\delta_2 R \tag{2.7}$$

$$\frac{dI}{dt} = (1-A)\lambda_1 S + \delta_1 \lambda_1 E + kE - (\mu + p + d) I + (1-f)\delta_2 \lambda_1 R \tag{2.8}$$

$$\frac{dR}{dt} = rV + pI - \mu R - \delta_2 \lambda_1 R \tag{2.9}$$

Where r is the rate at which vaccinated people developed immunity to tuberculosis disease infection and $\lambda_1 = \frac{\beta c I}{N}$ is the force of infection for tuberculosis disease.

An extensive review on the relevant literature review has revealed that while much research been done on transmission of tuberculosis, adequate research on the effects of case detection and resistance of tuberculosis is yet to be done. Though TB is a disease with vaccines readily available, it is still a disease that claims lots of lives. Several people have worked on the mathematical modelling of the spread of tuberculosis and have come to different conclusions on controlling the spread and transmission of the disease (Ogundile *et al*., 2018).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Formation of the Model

We first divide the human population at time t≥ 0, into six classes they are Susceptible $S(t)$, Expossed $E(t)$, Infected $I(t)$, Resistance to first line of treatment $R_1(t)$, Resistance to second line of treatmet $R_2(t)$, and the recorvered humans $R(t)$. The size of the human population is given by

$$N(t) = S(t) + E(t) + I(t) + R_1(t) + R_2(t) + R.$$

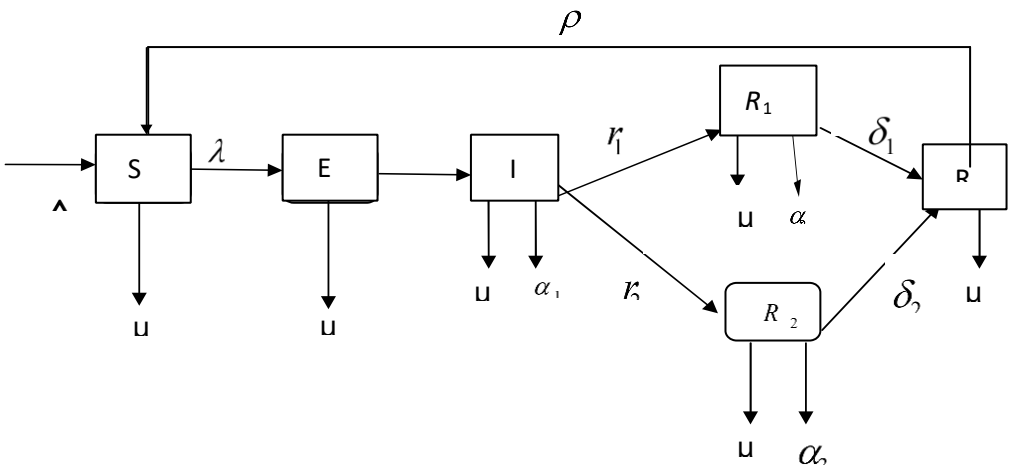

Figure 3.1 Schematic Diagram Showing the Flow of Tuberculosis Transmission Model

Table 3.1: Description of Parameters/Variables of the model

Parameter/Variables	Description
Λ	Recruitment rate
$S(t)$	Susceptible humans at time t
$E(t)$	Exposed human at time t
$I(t)$	Infected humans at time t
$R_1(t)$	Resistance class of individual to first line of treatment
$R_2(t)$	Resistance class of individual to second line of treatment
$R(t)$	Recovered humans at time t
η	Case detection rate
λ_1	Rate of transmission (detection)
λ_2	Rate of transmission (undetected)
μ	Natural death rate
γ	The rate at which the infected becomes infectious
ρ	Rate at which recovered individual loss their immunity
r_1	Resistance rate to first line of treatment
r_2	Resistance rate to second line of treatment
α_1	Diseases induced death rate
δ_1	Recovery rate after first line of treatment
δ_2	Recovery rate after second line of treatment
α_2	Diseases induced death rate after first line of treatment
α_3	Diseases induced death rate after second line of treatment

3.2 Basic assumptions of the model

1. The population is varying and homogenously mixed i.e. All people are equally likely to be infected by the infectious individual in case of contact.
2. Both detected and undetected case of individual transmit Tuberculosis at the different rate i.e. it is higher in undetected cases.
3. It is assumed that no permanent immunity to Tuberculosis.
4. Some infected individual delay treatment and moved to resistance classes.
5. Natural death occur in all the classes.

3.3 The model equation

$$\frac{dS}{dt} = \Lambda - \mu S - \left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) IS + \rho R \tag{3.1}$$

$$\frac{dE}{dt} = \left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) IS - \left(\mu + \gamma\right) E \tag{3.2}$$

$$\frac{dI}{dt} = \gamma E - \left(\mu + \alpha_1 + r_1 + r_2\right) I \tag{3.3}$$

$$\frac{dR_1}{dt} = r_1 I - \left(\mu + \alpha_2 + \delta_1\right) R_1 \tag{3.4}$$

$$\frac{dR_2}{dt} = r_2 I - \left(\mu + \alpha_3 + \delta_2\right) R_2 \tag{3.5}$$

$$\frac{dR}{dt} = \delta_1 R_1 + \delta_2 R_2 - \left(\mu + \rho\right) R \tag{3.6}$$

3.4 Invariant Region of the Model

The rate of total population is given by

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR_1}{dt} + \frac{dR_2}{dt} + \frac{dR}{dt} \tag{3.7}$$

$$\frac{dN}{dt} = \Lambda - \mu\left(S + E + I + R_1 + R_2 + R\right) - \left(\alpha_1 I + \alpha_2 R_1 + \alpha_3 R_2\right) \tag{3.8}$$

$$\frac{dN}{dt} \leq \Lambda - \mu\left(S + E + I + R_1 + R_2 + R\right) \tag{3.9}$$

$$\frac{dN}{dt} \leq \Lambda - \mu N \tag{3.10}$$

Where

$$N = S + E + I + R_1 + R_2 + R \tag{3.11}$$

Theorem 3.1: The system (3.1-3.6) has solutions which contain in the feasible region Ω for all $t \geq 0$.

Proof:

Let $\Omega = \left(S, E, I, R_1, R_2, R\right) \in \mathbb{R}^6$ be any solution of the system 3.1-3.6 with non-negative initial conditions then from equation (3.10) we have

$$\frac{dN}{dt} \leq \Lambda - \mu N \tag{3.12}$$

$$0 \leq N \leq \frac{\Lambda}{\mu} \tag{3.13}$$

We seek solution of the form

$$IF = e^{\int \mu dt} = e^{\mu t} \tag{3.17}$$

By multiplying through our equation (3.12) with the integrating factor we obtain

$$\left[Ne^{\mu t} \right]' \leq \Lambda e^{\mu t} \tag{3.18}$$

$\Rightarrow$

$$\Lambda - \mu N \geq Ce^{\mu t} \tag{3.19}$$

Therefore, all feasible solution of the human population of the model is in the region

$$\Omega = \left\{ \left(S, E, I, R_1, R_{2,} R \right) \in \mathbb{R}^6 : \left(S, E, I, R_1, R_{2,} R \right) \geq 0, N \leq \frac{\Lambda}{\mu} \right\} \tag{3.20}$$

3.5 Positivity of the solutions

Lemma 3.1: Let the initial solutions be $\left\{ S(0), E(0), I(0), R_1(0), R_2(0), R(0) \geq 0 \right\} \in \Omega$ then the solution $\left\{ S(t), E(t), I(t), R_1(t), R_2(t), R(t) \right\}$ of the system (3.1-3.6) is positive for all time $t \geq 0$.

Proof:

From equation (3.1) we have

$$\frac{dS}{dt} \geq -\mu S \tag{3.21}$$

By separating the variable and integrating equation (3.21) we have

$$\int \frac{dS}{S} \geq -\int \mu dt \tag{3.22}$$

$\Rightarrow$

$$S(t) \geq S(0)e^{-\mu t} \tag{3.23}$$

From (3.2) we have

$$\frac{dE}{dt} \geq -(\mu + \gamma) E \tag{3.24}$$

By separating the variable and integrating equation (3.24) we have

$$\int \frac{dE}{E} \geq -\int (\mu + \gamma) dt \tag{3.25}$$

$$\Rightarrow$$

$$E(t) \geq E(0) e^{-(\mu+\gamma)t} \tag{3.26}$$

From (3.3) we have

$$\frac{dI}{dt} \geq -(\mu + \alpha_1 + r_1 + r_2) I \tag{3.27}$$

By separating the variable and integrating equation (3.27) we have

$$\int \frac{dI}{I} \geq -\int (\mu + \alpha_1 + r_1 + r_2) dt \tag{3.28}$$

$$\Rightarrow$$

$$I(t) \geq I(0) e^{-(\mu+\alpha_1+r_1+r_2)t} \tag{3.29}$$

From (3.4) we have

$$\frac{dR_1}{dt} \geq -(\mu + \alpha_2 + \delta_1) R_1 \tag{3.30}$$

By separating the variable and integrating equation (3.30) we have

$$\int \frac{dR_1}{R_1} \geq \int -(\mu + \alpha_2 + \delta_1) dt \tag{3.31}$$

$$\Rightarrow$$

$$R_1(t) \geq R_1(0) e^{-(\mu+\alpha_2+\delta_1)t} \tag{3.32}$$

From (3.5) we have

$$\frac{dR_2}{dt} \geq -(\mu + \alpha_3 + \delta_2) R_2 \tag{3.33}$$

By separating the variable and integrating equation (3.33) we have

$$\int \frac{dR_2}{R_2} \geq \int -(\mu + \alpha_3 + \delta_2)\, dt \tag{3.34}$$

$\Rightarrow$

$$R_2(t) \geq R_2(0) e^{-(\mu+\alpha_3+\delta_2)t} \tag{3.35}$$

From (3.6) we have

$$\frac{dR}{dt} \geq -(\mu + \rho) R \tag{3.36}$$

By separating the variable and integrating equation (3.36) we have

$$\int \frac{dR}{R} \geq -\int (\mu + \rho) dt \tag{3.37}$$

$\Rightarrow$

$$R(t) \geq R(0) e^{-(\mu+\rho)t} \tag{3.38}$$

Therefore all the solution of the equation (3.1 -3.6) are positive for all time $t \geq 0$.

3.6 Basic Reproduction Number R_0

The basic reproduction number (R_0) is the average number of new infections that one infected case will generate during their entire infection life time. It is an important tool in determining whether the diseases persist or die out in population.

We use the next generation matrix to compute the basic reproduction number.

Basic reproduction number is the spectral radius $\rho\left(F_1V_1^{-1}\right)$ where the matrix F_i and V_i are the new infection terms and the remaining transfer terms respectively. The basic reproduction number is obtained as follow

Consider the differential equation for the diseases compartment

$$\frac{dE}{dt} = \lambda IS - \left(\mu + \gamma\right)E \tag{3.39}$$

$$\frac{dI}{dt} = \gamma E - \left(\mu + \alpha_1 + r_1 + r_2\right)I \tag{3.40}$$

$$\frac{dR_1}{dt} = r_1 I - \left(\mu + \alpha_2 + \delta_1\right)R_1 \tag{3.41}$$

$$\frac{dR_2}{dt} = r_2 I - \left(\mu + \alpha_3 + \delta_2\right)R_2 \tag{3.42}$$

Where $\lambda = \lambda_1\eta + \lambda_2(1-\eta)$

Let $X = \left(E, I, R_1, R_2\right)^T$ then the above system can be represented in matrix form as shown below: $\frac{dX_i}{dt} = F_i\left(X\right) - V_i\left(X\right)$ (3.43)

$$\text{Where } F\left(X\right)_i = \begin{pmatrix} \lambda SI \\ 0 \\ 0 \\ 0 \end{pmatrix}, \qquad V_i\left(X\right) = \begin{pmatrix} \left(\mu + \gamma\right)E \\ -\gamma E + \left(\mu + \alpha_1 + r_1 + r_2\right)I \\ -r_1 I + \left(\mu + \alpha_2 + \delta_1\right)R_1 \\ -r_2 I + \left(\mu + \alpha_3 + \delta_2\right)R_2 \end{pmatrix} \tag{3.44}$$

The Jacobian matrix of $F_i\left(X\right)$ and $V_i\left(X\right)$ at the diseases free equilibrium X_0 are,

$$\frac{dF_i(X_0)}{d(X)} = F_1 = \begin{pmatrix} 0 & \frac{\beta\Lambda}{\mu} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.45}$$

$$\frac{dV_i(X)}{d(X)} = V_1 = \begin{pmatrix} \mu+\gamma & 0 & 0 & 0 \\ -\gamma & \mu+\alpha_1+r_1+r_2 & 0 & 0 \\ 0 & -r_1 & \mu+\alpha_2+\delta_1 & 0 \\ 0 & 0 & 0 & -r_2 & 0 & \mu+\alpha_3+\delta_2 \end{pmatrix} \tag{3.46}$$

Now

$$V_1^{-1} = \begin{pmatrix} \frac{1}{\mu+\gamma} & 0 & 0 & 0 \\ \frac{\gamma}{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)} & \frac{1}{\mu+\alpha_1+r_1+r_2} & 0 & 0 \\ \frac{r_1\gamma}{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_2+\delta_1)} & \frac{r_1}{(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_2+\delta_1)} & \frac{1}{\mu+\alpha_2+\delta_1} & 0 \\ 0 & \frac{r_2\gamma}{(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_2+\delta_1)(\mu+\alpha_3+\delta_2)} & \frac{r_2}{(\mu+\alpha_1+r_1+r_2)(\mu+\alpha_3+\delta_2)} & 0 & \frac{1}{\mu+\alpha_3+\delta_2} \end{pmatrix} \tag{3.47}$$

The next generation matrix of the system is given by

$$F_1V_1^{-1} = \begin{pmatrix} \frac{\lambda\gamma\Lambda}{\mu(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)} & \frac{\lambda\Lambda}{\mu(\mu+\alpha_1+r_1+r_2)} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.48}$$

Thus our basic reproduction number is:

$$R_0 = \frac{\lambda\gamma\Lambda}{\mu(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)} \tag{3.49}$$

3.7 Equilibrium points of the model

To obtain the equilibrium points for the system above, we set each equation to be equal to zero as shown below

$$\frac{dS}{dt} = \Lambda - \mu S - (\lambda_1\eta + \lambda_2(1-\eta))IS + \rho R = 0 \tag{3.50}$$

$$\frac{dE}{dt} = (\lambda_1\eta + \lambda_2(1-\eta))IS - (\mu+\gamma)E = 0 \tag{3.51}$$

$$\frac{dI}{dt} = \gamma E - (\mu+\alpha_1+r_1+r_2)I = 0 \tag{3.52}$$

$$\frac{dR_1}{dt} = r_1 I - (\mu+\alpha_2+\delta_1)R_1 = 0 \tag{3.53}$$

$$\frac{dR_2}{dt} = r_2 I - (\mu+\alpha_3+\delta_2)R_2 = 0 \tag{3.54}$$

$$\frac{dR}{dt} = \delta_1 R_1 + \delta_2 R_2 - (\mu+\rho)R = 0 \tag{3.55}$$

Solving equation (3.50-3.55) above to get two equilibrium points, one being the diseases free equilibrium which the state at which no infection is present in the population and endemic equilibrium which is a state at which the infection persist in the population.

3.8 Disease Free Equilibrium of the Model

Let $X_0 = (S^0, E^0, I^0, R_1^0, R_2^0, R^0)$ Be the diseases free equilibrium points then the equation (3.50-3.55) above becomes

$$\Lambda - \mu S^0 - \left(\lambda_1\eta + \lambda_2(1-\eta)\right) I^0 S^0 + \rho R^0 = 0 \tag{3.56}$$

$$\left(\lambda_1\eta + \lambda_2(1-\eta)\right) I^0 S^0 - \left(\mu + \gamma\right) E^0 = 0 \tag{3.57}$$

$$\gamma E^0 - \left(\mu + \alpha_1 + r_1 + r_2\right) I^0 = 0 \tag{3.58}$$

$$r_1 I^0 - \left(\mu + \alpha_2 + \delta_1\right) R_1 = 0 \tag{3.59}$$

$$r_2 I^0 - \left(\mu + \alpha_3 + \delta_2\right) R^0{}_2 = 0 \tag{3.60}$$

$$\delta_1 R_1^0 + \delta_2 R^0{}_2 - \left(\mu + \rho\right) R^0 = 0 \tag{3.61}$$

From equation (3.57) we have

$$E^0 = \frac{\left(\lambda_1\eta + \lambda_2(1-\eta)\right) I^0 S^0}{\left(\mu + \gamma\right)} \tag{3.62}$$

Substituting (3.62) into (3.58) we have

$$\left(\frac{\gamma\left(\lambda_1\eta + \lambda_2(1-\eta)\right) S^0}{\left(\mu + \gamma\right)} - \left(\mu + \alpha_1 + r_1 + r_2\right) \right) I^0 = 0 \tag{3.63}$$

Which implies that

$$I^0 = 0 \tag{3.64}$$

or,

$$\left(\frac{\gamma\left(\lambda_1\eta + \lambda_2(1-\eta)\right) S^0}{\left(\mu + \gamma\right)} - \left(\mu + \alpha_1 + r_1 + r_2\right) \right) = 0 \tag{3.65}$$

Thus if $I^0 \neq 0$ we have

$$S^0 = \frac{\left(\mu + \gamma\right)\left(\mu + \alpha_1 + r_1 + r_2\right)}{\gamma\left(\lambda_1\eta + \lambda_2(1-\eta)\right)} \tag{3.66}$$

Putting equation (3.64) into (3.59) and (3.60) gives

$$R_1^0 = 0 \tag{3.67}$$

$$R_2^0 = 0 \tag{3.68}$$

Substituting equation (3.64) into (3.61)

$$R^0 = 0 \tag{3.69}$$

Putting (3.64) and (3.69) into (3.56) result in

$$S^0 = \frac{\Lambda}{\mu} \tag{3.70}$$

Thus diseases free equilibrium of the model is given by

$$X_0 = \left(S^0, E^0, I^0, R_1^0, R_2^0, R^0\right) = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0\right) \tag{3.71}$$

3.9 Endemic equilibrium $\left(S^*, E^*, I^*, R_1^*, R_2^*, R^*\right)$

We have $I \neq 0,\ \ E \neq 0, R_1 \neq 0 \ \ and \ \ \ R_2 \neq 0$

Thus from equation (3.66) we have

$$S^* = \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\gamma\left(\lambda_1\eta+\lambda_2(1-\eta)\right)} \tag{3.72}$$

From equation (3.50) we have

$$I^* = \frac{\Lambda-\mu S^*+\rho R^*}{\left(\lambda_1\eta+\lambda_2(1-\eta)\right)S^*} \tag{3.73}$$

From (3.51)

$$E^* = \frac{\left(\lambda_1\eta+\lambda_2(1-\eta)\right)S^*I^*}{(\mu+\gamma)} \tag{3.74}$$

From equation (3.53)

$$R_1^* = \frac{r_1 I^*}{\mu + \alpha_2 + \delta_1} \tag{3.75}$$

From (3.54) we have

$$R_2^* = \frac{r_2 I^*}{\mu + \alpha_3 + \delta_2} \tag{3.76}$$

From (3.55) we have

$$R^* = \frac{\delta_1 R^*_1 + \delta_2 R^*_2}{\mu + \rho} \tag{3.77}$$

Substitute (3.77) into (3.73) we have

$$I^* = \frac{\rho\left(\frac{\delta_1 R^*_1 + \delta_2 R^*_2}{\mu + \rho}\right) + \Lambda - \mu S^*}{\left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) S^*} \tag{3.78}$$

Again substituting both (3.75) and (3.76) into (3.78) and simplify we obtain

$$I^* = \frac{\left(\mu + \rho\right)\left(\Lambda - \mu S^*\right)}{\left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) S^* \left(\mu + \rho\right) - \rho\left(\frac{\delta_1 r_1}{\mu + \alpha_2 + \delta_1} + \frac{\delta_2 r_2}{\mu + \alpha_3 + \delta_2}\right)} \tag{3.79}$$

Substitute (3.79) into (3.74) we have

$$E^* = \frac{\left(\lambda_1 \eta + \lambda_2 \left(1-\eta\right)\right)\left(\mu + \rho\right)\left(\Lambda - \mu S^*\right) S^*}{\left(\mu + \gamma\right)\left(\left(\lambda_1 \eta + \lambda_2 (1-\eta)\right) S^* \left(\mu + \rho\right) - \rho\left(\frac{\delta_1 r_1}{\mu + \alpha_2 + \delta_1} + \frac{\delta_2 r_2}{\mu + \alpha_3 + \delta_2}\right)\right)} \tag{3.80}$$

Putting (3.79) into (3.75) we have

$$R_1^* = \frac{r_1(\mu+\rho)(\Lambda-\mu S^*)}{(\mu+\alpha_2+\delta_1)\left((\lambda_1\eta+\lambda_2(1-\eta))S^*(\mu+\rho)-\rho\left(\frac{\delta_1 r_1}{\mu+\alpha_2+\delta_1}+\frac{\delta_2 r_2}{\mu+\alpha_3+\delta_2}\right)\right)} \tag{3.81}$$

Putting (3.79) into (3.76) we have

$$R_2^* = \frac{r_2(\mu+\rho)(\Lambda-\mu S^*)}{(\mu+\alpha_3+\delta_2)\left((\lambda_2\eta+\lambda_3(1-\eta))S^*(\mu+\rho)-\rho\left(\frac{\delta_2 r_2}{\mu+\alpha_3+\delta_2}+\frac{\delta_3 r_3}{\mu+\alpha_3+\delta_2}\right)\right)} \tag{3.82}$$

Putting (3.81) and (3.82) into (3.77) we have

$$R^* = \frac{\left(\frac{\delta_1 r_1}{\mu+\alpha_2+\delta_1}+\frac{\delta_2 r_2}{\mu+\alpha_3+\delta_2}\right)(\mu+\rho)(\Lambda-\mu S^*)}{(\mu+\rho)\left((\lambda_1\eta+\lambda_2(1-\eta))S^*(\mu+\rho)-\rho\left(\frac{\delta_1 r_1}{\mu+\alpha_2+\delta_1}+\frac{\delta_2 r_2}{\mu+\alpha_3+\delta_2}\right)\right)} \tag{3.83}$$

Now let

$$b = \rho\left(\frac{\delta_1 r_1}{\mu+\alpha_2+\delta_1}+\frac{\delta_2 r_2}{\mu+\alpha_3+\delta_2}\right) \tag{3.84}$$

$$\lambda = \lambda_1\eta+\lambda_2(1-\eta) \tag{3.85}$$

Thus our endemic equilibrium points of the system above becomes

$$S^* = \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma} = \frac{\Lambda}{\mu R_0} \tag{3.86}$$

Putting (3.86) into (3.79-3.83) and expressed it in terms of reproduction number we have

$$E^* = \frac{\lambda \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}(\mu+\rho)\left(\Lambda - \mu\left(\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}\right)\right)}{(\mu+\gamma)\left(\lambda\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}(\mu+\rho)-b\right)}$$

$$E^* = \frac{\lambda K\mu(\mu+\alpha_1+r_1+r_2)(R_0-1)}{(\lambda K-b)} \tag{3.87}$$

$$I^* = \frac{(\mu+\rho)\left(\Lambda - \mu\left(\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}\right)\right)}{\lambda\left(\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}\right)(\mu+\rho)-b}$$

$$I^* = \frac{K\mu}{\lambda K-b}(R_0-1) \tag{3.88}$$

$$R_1^* = \frac{r_1(\mu+\rho)\left(\Lambda - \mu\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}\right)}{(\mu+\alpha_2+\delta_1)\left(\lambda\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}(\mu+\rho)-b\right)}$$

$$R_1^* = \frac{r_1K(R_0-1)}{(\mu+\alpha_2+\delta_1)(\lambda K-b)} \tag{3.89}$$

$$R_2^* = \frac{r_2(\mu+\rho)\left(\Lambda - \mu\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}\right)}{(\mu+\alpha_3+\delta_2)\left(\lambda\frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma}(\mu+\rho)-b\right)}$$

$$R_2^* = \frac{r_2 K\left(R_0 - 1\right)}{\left(\mu + \alpha_3 + \delta_2\right)\left(\lambda K - b\right)}$$

(3.90)

$$R^* = \frac{b\left(\Lambda - \mu\dfrac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\right)}{\rho\left(\lambda\dfrac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\left(\mu+\rho\right)-b\right)}$$

$$R^* = \frac{bK\left(R_0 - 1\right)}{\rho\left(\lambda K - b\right)} \tag{3.91}$$

Where $K = \dfrac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)\left(\mu+\rho\right)}{\lambda\gamma}$ (3.92)

3.10 Condition of existence and positivity of endemic equilibrium

The system will remain positive provided we have:

$$\frac{\Lambda - \mu\left(\dfrac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\right)}{\lambda\left(\dfrac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\right)\left(\mu+\rho\right)-b} > 0 \tag{3.93}$$

$$\Leftrightarrow \Lambda - \mu\left(\frac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\right) > 0 \quad \textit{and} \quad \lambda\left(\frac{\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)}{\lambda\gamma}\right)\left(\mu+\rho\right)-b > 0$$

$$\Leftrightarrow \lambda\gamma\Lambda > \mu\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right) \quad \textit{and} \quad \lambda K - b > 0$$

$$\Leftrightarrow \frac{\lambda\gamma\Lambda}{\mu\left(\mu+\gamma\right)\left(\mu+\alpha_1+r_1+r_2\right)} > 1 \quad \textit{and} \quad \lambda K - b > 0$$

$$\Leftrightarrow R_0 \succ 1 \quad \textit{and} \quad \lambda K > b \tag{3.94}$$

This expression in equation (3.94) is the condition for existence and positivity of the endemic equilibrium solution.

3.11 Stability analysis

The local dynamics of a general SEIRS model is determined by reproduction number R_0. If $R_0 < 1$, then each infected individual in its entire period of infectiousness will produce less than one infected individual on average. This means that the diseases will be wiped out of the population. If $R_0 > 1$, then each infected individual in its entire infectious period having contact with susceptible individuals will produce more than one infected individuals in its entire infectious period having contact with susceptible individuals will produce more than one infected individual implying that the diseases persist in the population. If $R_0 = 1$ and this is defined as the diseases threshold, then one individual will infects one more individuals.

3.12 Local Stability of Disease Free Equilibrium

Theorem 3.2. If $R_0 < 1$ then the diseases free equilibrium of the model is locally asymptotically stable and unstable if $R_0 \geq 1$.

Proof: We use the jacobian stability approach to prove the stability of the diseases free equilibrium.

$$J(E)=\begin{pmatrix} -(\mu+\lambda I) & 0 & -\lambda S & 0 & 0 & \rho \\ \lambda I & -(\mu+\gamma) & \lambda S & 0 & 0 & 0 \\ 0 & \gamma & -(\mu+\alpha_1+r_1+r_2) & 0 & 0 & 0 \\ 0 & 0 & r_1 & -(\mu+\alpha_2+\delta_1) & 0 & 0 \\ 0 & 0 & r_2 & 0 & -(\mu+\alpha_3+\delta_2) & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & -(\mu+\rho) \end{pmatrix} \quad (3.95)$$

At the diseases free equilibrium we have $I = E = R_1 = R_2 = R = 0$ *and* $S = \frac{\Lambda}{\mu}$

Thus the Jacobian matrix at disease free equilibrium is given by:

$$J(E_0)=\begin{pmatrix} -\mu & 0 & -\frac{\lambda\Lambda}{\mu} & 0 & 0 & \rho \\ 0 & -(\mu+\gamma) & \frac{\lambda\Lambda}{\mu} & 0 & 0 & 0 \\ 0 & \gamma & -(\mu+\alpha_1+r_1+r_2) & 0 & 0 & 0 \\ 0 & 0 & r_1 & -(\mu+\alpha_2+\delta_1) & 0 & 0 \\ 0 & 0 & r_2 & 0 & -(\mu+\alpha_3+\delta_2) & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & -(\mu+\rho) \end{pmatrix} \quad (3.96)$$

Let $K = \mu+\alpha_1+r_1+r_2$

$$J(E_0)=\begin{pmatrix} -\mu & 0 & -\frac{\lambda\Lambda}{\mu} & 0 & 0 & \rho \\ 0 & -(\mu+\gamma) & \frac{\lambda\Lambda}{\mu} & 0 & 0 & 0 \\ 0 & \gamma & -K & 0 & 0 & 0 \\ 0 & 0 & r_1 & -(\mu+\alpha_2+\delta_1) & 0 & 0 \\ 0 & 0 & r_2 & 0 & -(\mu+\alpha_3+\delta_2) & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & -(\mu+\rho) \end{pmatrix} \tag{3.97}$$

The characteristic matrix is given by

$$J(E_0)=\begin{pmatrix} \lambda_i+\mu & 0 & -\frac{\lambda\Lambda}{\mu} & 0 & 0 & \rho \\ 0 & \lambda_i+\mu+\gamma & \frac{\lambda\Lambda}{\mu} & 0 & 0 & 0 \\ 0 & \gamma & \lambda_i+K & 0 & 0 & 0 \\ 0 & 0 & r_1 & \lambda_i+\mu+\alpha_2+\delta_1 & 0 & 0 \\ 0 & 0 & r_2 & 0 & \lambda_i+\mu+\alpha_3+\delta_2 & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & \lambda_i+\mu+\rho \end{pmatrix} \tag{3.98}$$

Thus the Eigenvalues of the jacobian matrix is given by

$$\lambda_1=-\mu<0 \tag{3.99}$$

$$\lambda_2=-(\mu+\alpha_2+\delta_1)<0 \tag{3.100}$$

$$\lambda_3=-(\mu+\alpha_3+\delta_2)<0 \tag{3.101}$$

$$\lambda_4=-(\mu+\rho)<0 \tag{3.102}$$

$$\lambda_5=-\frac{1}{2}\left(K+\mu+\gamma+\sqrt{\frac{4\lambda\gamma\Lambda}{\mu}+K^2-2K\mu-2K\gamma+\mu^2+2\mu\gamma+\gamma^2}\right)<0 \tag{3.103}$$

If

$$\lambda_6 = \frac{1}{2}\left(-\left(K+\mu+\gamma\right) + \sqrt{\frac{4\lambda\gamma\Lambda}{\mu} + K^2 - 2K\mu - 2K\gamma + \mu^2 + 2\mu\gamma + \gamma^2} \right) < 0 \tag{3.104}$$

This implies that

$$\left(K+\mu+\gamma\right)^2 > \frac{4\lambda\gamma\Lambda}{\mu} + K\left(\left(K-2(\mu+\gamma)\right)\right) + \left(\mu+\gamma\right)^2 \tag{3.105}$$

Let $Z = \mu + \gamma$ (3.106)

$$\left(K+Z\right)^2 > \frac{4\lambda\gamma\Lambda}{\mu} + K\left(K-2Z\right) + Z^2 \tag{3.107}$$

$\Rightarrow$

$$\frac{4\lambda\gamma\Lambda}{\mu} + K\left(K-2Z\right) + Z^2 - \left(K+Z\right)^2 < 0 \tag{3.108}$$

$\Rightarrow$

$$\frac{4\lambda\gamma\Lambda}{\mu} + K^2 + Z^2 - 2KZ - K^2 - 2KZ - Z^2 < 0 \tag{3.109}$$

$\Rightarrow$

$$\frac{4\beta\gamma\Lambda}{\mu} - 4KZ < 0 \tag{3.110}$$

Putting $Z = \mu + \gamma$ and $K = \mu + \alpha_1 + r_1 + r_2$ into equation (3.110) we have

$$\frac{4\lambda\gamma\Lambda}{\mu} - 4\left(\mu+\alpha_1+r_1+r_2\right)\left(\mu+\gamma\right) < 0 \tag{3.111}$$

$\Rightarrow$

$$\frac{4}{\left(\mu+\alpha_1+r_1+r_2\right)\left(\mu+\gamma\right)}\left(\frac{\lambda\gamma\Lambda}{\mu\left(\mu+\alpha_1+r_1+r_2\right)\left(\mu+\gamma\right)} - 1 \right) < 0 \tag{3.112}$$

But from equation (3.49) we have

$$R_0 = \frac{\lambda\gamma\Lambda}{\mu(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}$$

Thus we have

$$\frac{4}{(\mu+\alpha_1+r_1+r_2)(\mu+\gamma)}(R_0-1)<0 \qquad (3.113)$$

Equation (3.113) will hold if $R_0<1$

Thus all eigenvalues of the Jacobian Matrix above has negative real part if $R_0<1$

Hence from Routh Hurwitz stability criteria we conclude that the diseases free equilibrium is locally asymptotically stable.

3.13 Global stability of the diseases free equilibrium.

Theorem 3.4: If $R_0 \le 1$ then the diseases free equilibrium of the system is globally asymptotically stable on Ω.

Proof. By constructing an appropriate Lyapunov function $V=(S,E,I,R_1,R_2,R)$ on the positively invariant compact set Ω.

Defined

$$V=(S,E,I,R_1,R_2,R)=\gamma E+(\mu+\gamma)I. \qquad (3.114)$$

Differentiate equation (3.127) by t we have

$$\frac{dV}{dt}=\gamma\frac{dE}{dt}+(\mu+\gamma)\frac{dI}{dt}. \qquad (3.115)$$

Substitute equation (3.2) and (3.3) into (3.115) we have

$$\frac{dV}{dt} = \gamma\left(\lambda IS - (\mu+\gamma)E\right) + (\mu+\gamma)\left(\gamma E - (\mu+\alpha_1+r_1+r_2)\right)I \tag{3.116}$$

$$\frac{dV}{dt} = \lambda\gamma IS - \gamma(\mu+\gamma)E + \gamma(\mu+\gamma)E - (\mu+\gamma)(\mu+\alpha_1+r_1+r_2)I \tag{3.117}$$

$$\frac{dV}{dt} = \lambda\gamma IS - (\mu+\gamma)(\mu+\alpha_1+r_1+r_2)I \tag{3.118}$$

$$\frac{dV}{dt} = \left[\lambda\gamma\frac{\Lambda}{\mu} - (\mu+\gamma)(\mu+\alpha_1+r_1+r_2)\right]I \tag{3.119}$$

$$\frac{dV}{dt} = (\mu+\gamma)(\mu+\alpha_1+r_1+r_2)\left(\frac{\lambda\gamma\Lambda}{\mu(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)} - 1\right)I \tag{3.120}$$

$$\frac{dV}{dt} = (\mu+\gamma)(\mu+\alpha_1+r_1+r_2)(R_0-1)I \tag{3.121}$$

Which is strictly decreasing when $R_0 < 1$

i.e

$$\frac{dV}{dt} < 0 \ \ if \ \ R_0 < 1$$

(3.122)

and

$$\frac{dV}{dt} = 0 \quad \text{If and only if} \quad E = 0, I = 0, R_1 = 0, R_2 = 0 \ and \ R_0 = 1$$

(3.123)

Defining the set $E_0 = \left\{(E, I, R_1, R_2) \in \Omega : \frac{dL}{dt} = 0\right\}$ the largest invariant set E_0 is contained in the set thus by LaSalle invariant principle the diseases free equilibrium is globally asymptotically stable.

Hence the proof is complete.

3.14 Local stability of the endemic equilibrium

Theorem 3.3: The endemic equilibrium state of the system (3.1-3.6) is locally asymptotically stable if

$R_0 > 1$.

Proof:

Using jacobian stability approach we consider the Jacobian matrix of (3.1-3.6) at endemic equilibrium points

$$J(E) = \begin{pmatrix} -(\mu+\lambda I^*) & 0 & -\lambda S^* & 0 & 0 & \rho \\ \lambda I^* & -(\mu+\gamma) & \lambda S^* & 0 & 0 & 0 \\ 0 & \gamma & -(\mu+\alpha_1+r_1+r_2) & 0 & 0 & 0 \\ 0 & 0 & r_1 & -(\mu+\alpha_2+\delta_1) & 0 & 0 \\ 0 & 0 & r_2 & 0 & -(\mu+\alpha_3+\delta_2) & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & -(\mu+\rho) \end{pmatrix} \quad (3.124)$$

Let K1= $\mu+\alpha_1+r_1+r_2$, K2= $\mu+\alpha_2+\delta_1$, K3= $\mu+\alpha_3+\delta_2$, K4= $\mu+\rho$, K5= $\mu+\gamma$

Also at the endemic equilibrium we have

$$S^* = \frac{(\mu+\gamma)(\mu+\alpha_1+r_1+r_2)}{\lambda\gamma} = \frac{\Lambda}{\mu R_0} \quad (3.125)$$

$$I^* = \frac{K\mu}{\lambda K - b}(R_0 - 1) = A(R_0 - 1) \quad (3.126)$$

Where $A = \frac{K\mu}{\lambda K - b}$

We are sure that A is always positive since both K and μ are positive parameter and from equation (3.94)

We have that $R_0 > 1$ implies $\lambda K - b > 0$

Putting equation (3.125) and (3.126) into (3.124) we obtain

$$J(E) = \begin{pmatrix} -(\mu + \lambda A(R_0 - 1)) & 0 & \frac{-\lambda\Lambda}{\mu R_0} & 0 & 0 & \rho \\ \lambda A(R_0 - 1) & -K_5 & \frac{\lambda\Lambda}{\mu R_0} & 0 & 0 & 0 \\ 0 & \gamma & -K_1 & 0 & 0 & 0 \\ 0 & 0 & r_1 & -K_2 & 0 & 0 \\ 0 & 0 & r_2 & 0 & -K_3 & 0 \\ 0 & 0 & 0 & \delta_1 & \delta_2 & -K_4 \end{pmatrix} \quad (3.127)$$

By reducing equation (3.127) to upper triangular matrix using Gaussian elimination method we have

$$J(E) = \begin{pmatrix} -(\mu + \lambda A(R_0 - 1)) & 0 & \frac{-\lambda\Lambda}{\mu R_0} & 0 & 0 & \rho \\ 0 & -K_5 & \frac{\lambda\Lambda}{(A\lambda(R_0 - 1) + \mu)R_0} & 0 & 0 & \frac{\lambda A(R_0 - 1)\rho}{(A\lambda(R_0 - 1) + \mu)} \\ 0 & 0 & -\frac{ZR_0(R_0 - 1)}{K_5(A\lambda(R_0 - 1) + \mu)R_0} & 0 & 0 & \frac{\lambda A\gamma(R_0 - 1)\rho}{K_5(A\lambda(R_0 - 1) + \mu)} \\ 0 & 0 & 0 & -K_2 & 0 & \frac{\lambda AR_0 r_1\gamma(R_0 - 1)\rho}{ZR_0(R_0 - 1)} \\ 0 & 0 & 0 & 0 & -K_3 & \frac{\lambda AR_0 r_2\gamma(R_0 - 1)\rho}{Z(R_0 - 1)} \\ 0 & 0 & 0 & 0 & 0 & -\frac{R_0(K_3K_4K_2Z - (M_1 + M_2))(R_0 - 1)}{K_2K_3(Z(R_0 - 1))} \end{pmatrix} \quad (3.128)$$

Where $Z = AK_1K_5\lambda$ *and* $M_1 + M_2 = \left(K_3\delta_1 r_1 + K_2\delta_2 r_2\right)\gamma\lambda A\rho$

Thus the Eigenvalues of the reduced Jacobian matrix is

$$\lambda_1 = -K_5 < 0 \tag{3.129}$$

$$\lambda_2 = -K_3 < 0 \tag{3.130}$$

$$\lambda_3 = -K_2 < 0 \tag{3.131}$$

$$\lambda_4 = -\left(\mu + \lambda A(R_0 - 1)\right) < 0 \quad If \;\; R_0 > 1 \tag{3.132}$$

$If \;\; R_0 > 1$

$$\lambda_5 = -\frac{Z(R_0 - 1)}{K_5\left(A\lambda(R_0 - 1) + \mu\right)R_0} < 0 \tag{3.133}$$

$$\lambda_6 = -\frac{R_0\left(K_3K_4K_2Z - (M_1 + M_2)\right)(R_0 - 1)}{K_2K_3\left(Z(R_0 - 1)\right)} < 0 \tag{3.134}$$

$$if \;\; R_0 > 1 \quad and \quad K_3K_4K_5Z > M_1 + M_2 \tag{3.135}$$

Which verified the local stability of the endemic equilibrium $if \;\; R_0 > 1.$

The epidemiological implication of this is that the diseases persist in the population $if \;\; R_0 > 1$

3.15 Global Stability of Diseases Endemic Equilibrium

Theorem 3.5: The endemic equilibrium $\Phi = \left(S^*, E^*, I^*, R_1^*, R_1^*, R^*\right)$ is globally asymptotically stable $\Omega \; If \;\; R_0 > 1$.

Proof:

We establish the stability of endemic equilibrium by constructing Lyapunuv function

$$V(S,E,I,R_1,R_2,R)=\begin{bmatrix}\lambda_1\left[S-S^*-S^*\ln\left(\frac{S}{S^*}\right)\right]+\lambda_2\left[E-E^*-E^*\ln\left(\frac{E}{E^*}\right)\right]+\\ \lambda_3\left[I-I^*-I^*\ln\left(\frac{I}{I^*}\right)\right]+\lambda_4\left[R_1-R_1^*-R_1^*\ln\left(\frac{R_1}{R_1^*}\right)\right]+\\ \lambda_5\left[R_2-R_2^*-R_2^*\ln\left(\frac{R_2}{R_2^*}\right)\right]+\lambda_6\left[R-R^*-R^*\ln\left(\frac{R}{R^*}\right)\right]\end{bmatrix} \quad 3.136$$

Where $\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,\lambda_6$ are positive constant.

Taking the derivative of the Lyapunov function V above we have

$$\frac{dV}{dt}=\begin{bmatrix}\lambda_1\left(1-\frac{S^*}{S}\right)\frac{dS}{dt}+\lambda_2\left(1-\frac{E^*}{E}\right)\frac{dE}{dt}+\lambda_3\left(1-\frac{I^*}{I}\right)\frac{dE}{dt}+\\ \lambda_4\left(1-\frac{R_1^*}{R_1}\right)\frac{dR_1}{dt}+\lambda_5\left(1-\frac{R_2^*}{R_2}\right)\frac{dR_2}{dt}+\lambda_6\left(1-\frac{R^*}{R}\right)\frac{dR}{dt}\end{bmatrix} \quad (3.136)$$

By substituting equation 3.1-3.6 into (3.128) and using the relation obtain from (3.1-3.6) as

$$\Lambda+\rho R^*=\left(\lambda I^*+\mu\right)S^* \quad (3.137)$$

$$\lambda I^*S^*=\left(\mu+\gamma\right)E^* \quad (3.138)$$

$$\gamma E^*=\left(\mu+\alpha_1+r_1+r_2\right)I^* \quad (3.139)$$

$$r_1I^*=\left(\mu+\alpha_2+\delta_1\right)R_1^* \quad (3.140)$$

$$r_2 I^* = \left(\mu + \alpha_3 + \delta_2\right) R_2^* \tag{3.141}$$

$$\delta_1 R_1^* + \delta_2 R_2^* = \left(\mu + \rho\right) R^* \tag{3.142}$$

We obtain

$$\frac{dV}{dt} = -\left[\begin{array}{c} \frac{\lambda_1\left(S - S^*\right)^2\left(\lambda I^* + \mu\right)}{S} + \frac{\lambda_2\left(E - E^*\right)^2\left(\mu + \gamma\right)}{E} + \frac{\lambda_3\left(I - I^*\right)^2\left(\mu + \alpha_1 + r_1 + r_2\right)}{I} + \\ \frac{\lambda_4\left(R_1 - R_1^*\right)^2\left(\mu + \alpha_2 + \delta_1\right)}{R_1} + \frac{\lambda_5\left(R_2 - R_2^*\right)^2\left(\mu + \alpha_3 + \delta_2\right)}{R_2} + \frac{\lambda_6\left(R - R^*\right)^2\left(\mu + \rho\right)}{R} \end{array}\right] \tag{3.143}$$

From equation (3.118) we have $I^* = A(R_0 - 1)$ thus equation (3.143) becomes

$$\frac{dV}{dt} = -\left[\begin{array}{c} \frac{\lambda_1\left(S - S^*\right)^2\left(\lambda A(R_0 - 1) + \mu\right)}{S} + \frac{\lambda_2\left(E - E^*\right)^2\left(\mu + \gamma\right)}{E} + \frac{\lambda_3\left(I - I^*\right)^2\left(\mu + \alpha_1 + r_1 + r_2\right)}{I} + \\ \frac{\lambda_4\left(R_1 - R_1^*\right)^2\left(\mu + \alpha_2 + \delta_1\right)}{R_1} + \frac{\lambda_5\left(R_2 - R_2^*\right)^2\left(\mu + \alpha_3 + \delta_2\right)}{R_2} + \frac{\lambda_6\left(R - R^*\right)^2\left(\mu + \rho\right)}{R} \end{array}\right] \tag{3.144}$$

$\Rightarrow$

$\frac{dV}{dt} < 0 \;\; if \;\; R_0 > 1$

and

$\frac{dV}{dt} = 0 \;\; iff \;\; S = S^*, \; E = E^*, \; I = I^*, \;\; R_1 = R_1^*, \; R_2 = R_2^*, \; and \;\; R = R^*$

Thus the largest compact invariant set in $\Phi = \left(S^*, E^*, I^*, R_1^*, R_1^*, R^*\right) \in \Omega : \frac{dV}{dt} = 0$ is the singleton set Φ where Φ is the endemic equilibrium. Thus Φ is globally asymptotically stable in the interior of the region Ω.

Hence the proof is complete.

3.16 Homotopy Solution of the model

To show the basic concept of the method of homotopy method

He (2000) considered the following non-linear differential equation.

$$L(u) + N(u) = f(r), \qquad r \in \Omega \tag{3.145}$$

With the boundary conditions

$$B\left(u, \frac{\partial u}{\partial n}\right) = 0, \quad r \in \Gamma \tag{3.146}$$

Where L is a linear operator, N is a non-linear operator, B is the boundary operator, Γ is the boundary of the domain Ω and $f(r)$ is a known analytic function.

By the Homotopy Pertubation technique, He construct a homotopy:

$$V(r, p) : \Omega \times [0,1] \to R \tag{3.147}$$

Which satisfy

$$H(v, p) = (1-p)\left[L(v) - L(u_0)\right] + p\left[L(v) + N(v) - f(r)\right] = 0 \tag{3.148}$$

Where $r \in \Omega$, $p \in [0,1]$ is an impending parameter and u_0 is an initial approximation which satisfy the boundary conditions.

It can be assumed that the solution of equation (3.98) can be written as power series in p as follows

$$V = \lim_{p \to 1} U = U_0 + pU_1 + p^2 U_2 + ... \tag{3.149}$$

The series is convergent in most cases, however the convergent rate depends on the non-linear operator A(v).

$$\frac{dS}{dt} + \lambda IS + \mu S - \Lambda - \rho R = 0 \tag{3.150}$$

$$\frac{dE}{dt} + (\mu + \gamma) E - \lambda IS = 0 \tag{3.151}$$

$$\frac{dI}{dt} + K_1 I - \gamma E = 0 \tag{3.152}$$

$$\frac{dR_1}{dt} + K_2 R_1 - r_1 I = 0 \tag{3.153}$$

$$\frac{dR_2}{dt} + K_3 R_2 - r_2 I = 0 \tag{3.154}$$

$$\frac{dR}{dt}+(\mu+\rho)R-\delta_1 R_1-\delta_2 R_2=0 \tag{3.155}$$

With the following initial conditions

$$S(0)=S_o, E(0)=E_o, I(0)=I_{o,}\, R_1(0)=(R_1)_o, R_2(0)=(R_2)_o, R(0)=R_O \tag{3.156}$$

Applying HPM to (3.150)

$$(1-p)\frac{dS}{dt}+p\left(\frac{dS}{dt}+(\lambda I+\mu)S-\Lambda-\rho R\right)=0 \tag{3.157}$$

Defining

$$S=u_o+pu_1+p^2u_2+\ldots \tag{3.158}$$

$$E=v_o+pv_1+p^2v_2+\ldots \tag{3.159}$$

$$I=w_0+pw_1+p^2w_2+\ldots \tag{3.160}$$

$$R_1=x_0+px_1+p^2x_2+\ldots \tag{3.161}$$

$$R_2=y_0+py_1+p^2y_2+\ldots \tag{3.162}$$

$$R=z_0+pz_1+p^2z_2+\ldots \tag{3.163}$$

By substituting equation (3.158), (3.160) and (3.163) into (3.157) we have

$$\left(u_0^{'}+pu_1^{'}+p^2u_2^{'}+\ldots\right)+p\left[\begin{array}{r}\left(\lambda\left(w_0+pw+p^2w_2+\ldots\right)+\mu\right)\left(u_0+pu_1+p^2u_2+\ldots\right)\\ -\Lambda-\rho\left(z_0+pz_1+p^2z_2+\ldots\right)\end{array}\right]=0 \tag{3.164}$$

By collecting the coefficient of independent power of p in equation (3.164) we have

$$p^0 : \mathrm{u}_0^{'} = 0 \tag{3.165}$$

$$p^1 : u_1^{'} + \lambda w_0 u_0 - \Lambda - \rho z_0 + \mu u_0 = 0 \tag{3.166}$$

$$p^2 : \mathrm{u}_2^{'} + \lambda w_0 u_1 + \beta u_0 + \mu u_1 - \rho z_1 = 0 \tag{3.167}$$

Applying HPM to equation (3.151) we have

$$(1-P)\frac{dE}{dt} + p\left(\frac{dE}{dt} + (\mu+\gamma)E - \lambda IS\right) = 0 \tag{3.168}$$

$$\left(v_0^{'} + pv_1^{'} + p^2 v_2^{'} + \cdots\right) + p\left[\begin{array}{l}(\mu+\gamma)\left(v_0 + pv_1 + p^2 v_2\right) - \\ \lambda(\mathrm{w}_0 + pw_1 + p^2 w_2 + \cdots)\left(u + \mathrm{pu}_1 + \mathrm{pu}_2 + \cdots\right)\end{array}\right] = 0 \tag{3.169}$$

By collecting coefficient of independent power of p in equation (3.169) we have

$$p^0 : \mathrm{v}_0^{'} = 0 \tag{3.170}$$

$$p^1 : \mathrm{v}_1^{'} + (\mu+\gamma)v_0 - \lambda w_0 u_0 = 0 \tag{3.171}$$

$$p^2 : \mathrm{v}_2^{'} + (\mu+\gamma)v_1 - \lambda\left(w_0 u_1 + w_1 u_0\right) = 0 \tag{3.172}$$

Applying HPM to equation (3.152)

$$(1-P)\frac{dI}{dt} + p\left(\frac{dI}{dt} + K1I - \gamma E\right) = 0 \tag{3.173}$$

$$\left(w_0^{'} + pw_1^{'} + p^2 w_2^{'} + \cdots\right) + p\left[K1\left(w_0 + pw_1 + p^2 w_2 + \ldots\right) - \gamma\left(v_1 + pv_1 + p^2 v_2 + \cdots\right)\right] = 0 \tag{3.174}$$

$$p^0 : \mathrm{w}_0^{'} = 0 \tag{3.175}$$

$$p^1 : \mathrm{w}_1^{'} + w_0 K1 - \gamma v_0 = 0 \tag{3.176}$$

$$p^2 : \mathrm{w}_2^{'} + K1 w_1 - \gamma v_1 = 0 \tag{3.177}$$

Applying HPM to equation (3.153) we have

$$(1-P)\frac{dR_1}{dt}+p\left(\frac{dR_1}{dt}+K_2R_1-r_1I\right)=0 \tag{3.178}$$

$$\left(x_0^{'}+px_1^{'}+p^2x_2^{'}+\cdots\right)+p\left[K_2\left(x_0+px_1+p^2x_2+\ldots\right)-r_1\left(w_0+pw_1+p^2w_2+\cdots\right)\right]=0 \tag{3.179}$$

$$p^0:x_0^{'}=0 \tag{3.180}$$

$$p^1:x_1^{'}+x_0K_2-r_1w_0=0 \tag{3.181}$$

$$p^2:x_2^{'}+K_2x_1-r_1w_1=0 \tag{3.182}$$

Applying HPM to equation (3.154)

$$(1-P)\frac{dR_2}{dt}+p\left(\frac{dR_2}{dt}+K_3R_2-r_2I\right)=0 \tag{3.183}$$

$$\left(y_0^{'}+py_1^{'}+p^2y_2^{'}+\cdots\right)+p\left[K_3\left(y_0+py_1+p^2y_2+\ldots\right)-r_2\left(w_0+pw_1+p^2w_2+\cdots\right)\right]=0 \tag{3.184}$$

$$p^0:y_0^{'}=0 \tag{3.185}$$

$$p^1:y_1^{'}+y_0K_3-r_2w_0=0 \tag{3.186}$$

$$p^2:y_2^{'}+K_3x_y-r_2w_1=0 \tag{3.187}$$

Applying HPM to equation (3.155)

$$(1-P)\frac{dR}{dt}+p\left(\frac{dR}{dt}+(\mu+\rho)R-\delta_1R_1-\delta_2R_2\right)=0 \tag{3.188}$$

$$\left(z_0^{'}+pz_1^{'}+p^2z_2^{'}+\cdots\right)+p\begin{bmatrix}(\mu+\rho)\left(z_0+pz_1+p^2z_2+\ldots\right)-\delta_1\left(x_0+px_1+p^2x_2+\cdots\right)\\-\delta_2\left(y_0+py_1+p^2y_2+\cdots\right)\end{bmatrix}=0 \tag{3.189}$$

By collecting the coefficient of independent power of p in equation (3.189) we have

$$p^0:z_0^{'}=0 \tag{3.190}$$

$$p^1:z_1^{'}+(\mu+\rho)z_0-\delta_1x_0-\delta_2y_0=0 \tag{3.191}$$

$$p^2:z_2^{'}+(\mu+\rho)z_1-\delta_1x_1-\delta_2y\ =0 \tag{3.192}$$

Solving equation (3.165), (3.170), (3.175) (3.180), (3.185), (3.190) we obtained

$$u_0 = S_0 \tag{3.193}$$
$$v_0 = E_0 \tag{3.194}$$
$$w_0 = I_0 \tag{3.195}$$
$$x_0 = \left(R_1\right)_0 \tag{3.196}$$
$$y_0 = \left(R_2\right)_0 \tag{3.197}$$
$$z_0 = R_0 \tag{3.198}$$

By substituting equations (3.193) - (3.198) into equations (3.166), (3.171), (3.176), (3.181), (3.186) and (3.191) and integrating, we obtain the following equations

$$\mathrm{u}_1 = (\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0)t \tag{3.199}$$
$$v_1 = \left(\lambda I_0 S_0 - (\mu + \gamma)E_0\right)t \tag{3.200}$$
$$w_1 = \left(\gamma E_0 - K_1 I_0\right)t \tag{3.201}$$
$$x_1 = \left(r_1 I_0 - K_2 (R_1)_0\right)t \tag{3.202}$$
$$y_1 = \left(r_2 I_0 - K_3 (R_2)_0\right)t \tag{3.203}$$
$$z_1 = \left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0 - \left(\mu + \rho\right)R_0\right)t \tag{3.204}$$

By substituting equations (3.199 - 3.204) into equations (3.167), (3.172), (3.177), (3.182), (3.187) and (3.192) and integrating, we obtain the following equations

$$u_2 = \left[\begin{array}{r} \rho\left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0 - \left(\mu + \rho\right)R_0\right) - \lambda I_0 (\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0) \\ - \lambda\left(\gamma E_0 - K_1 I_0\right)S_0 - \mu\left(\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0\right) \end{array}\right]\frac{t^2}{2} \tag{3.205}$$
$$v_2 = \left[\begin{array}{r} \lambda w_0\left(\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S\right) - (\mu + \gamma)\left(\lambda I_0 S_0 - (\mu + \gamma)E_0\right) \\ - S_0\left(\gamma E_0 - K_1 I_0\right) \end{array}\right]\frac{t^2}{2} \tag{3.206}$$
$$w_2 = \left[\gamma\left(\lambda I_0 S_0 - (\mu + \gamma)E_0\right) - K_1\left(\gamma E_0 - K_1 I_0\right)\right]\frac{t^2}{2} \tag{3.207}$$
$$x_2 = \left[r_1\left(\gamma E_0 - K_1 I_0\right) - K_2\left(r_1 I_0 - K_2 (R_1)_0\right)\right]\frac{t^2}{2} \tag{3.208}$$
$$y_2 = \left[r_2\left(\gamma E_0 - K_1 I_0\right) - K_3\left(r_2 I_0 - K_3 (R_2)_0\right)\right]\frac{t^2}{2} \tag{3.209}$$
$$z_2 = \left[\delta_1\left(r_2 I_0 - K_3 (R_2)_0\right) + \delta_2\left(r_2 I_0 - K_3 (R_2)_0\right) - (\mu + \rho)\left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0\right)\right]\frac{t^2}{2} \tag{3.210}$$

By substituting equations (3.205 - 3.210) into (3.158) - (3.163) and set p=1 we have

$$\lim_{p\to 1} u = u_0 + u_1 + u_2$$

$$S(t) = S_0 + (\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0)t + \begin{bmatrix} \rho\left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0 - (\mu+\rho) R_0\right) - \lambda I_0 (\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0) \\ -\lambda\left(\gamma E_0 - K_1 I_0\right) S_0 - \mu\left(\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S_0\right) \end{bmatrix} \frac{t^2}{2} \quad (3.211)$$

$$E(t) = E_0 + \left(\lambda I_0 S_0 - (\mu+\gamma) E_0\right)t + \begin{bmatrix} \lambda w_0 \left(\Lambda + \rho z_0 - \lambda I_0 S_0 - \mu S\right) - (\mu+\gamma)\left(\lambda I_0 S_0 - (\mu+\gamma) E_0\right) \\ -S_0\left(\gamma E_0 - K_1 I_0\right) \end{bmatrix} \frac{t^2}{2} \quad (3.212)$$

$$I(t) = I_0 + \left(\gamma E_0 - K_1 I_0\right)t + \left[\gamma\left(\lambda I_0 S_0 - (\mu+\gamma) E_0\right) - K_1\left(\gamma E_0 - K_1 I_0\right)\right]\frac{t^2}{2} \quad (3.213)$$

$$R_1(t) = (R_1)_0 + \left(r_1 I_0 - K_2 (R_1)_0\right)t + \left[r_1\left(\gamma E_0 - K_1 I_0\right) - K_2\left(r_1 I_0 - K_2 (R_1)_0\right)\right]\frac{t^2}{2} \quad (3.214)$$

$$R_2(t) = (R_2)_0 + \left(r_2 I_0 - K_3 (R_2)_0\right)t + \left[r_2\left(\gamma E_0 - K_1 I_0\right) - K_3\left(r_2 I_0 - K_3 (R_2)_0\right)\right]\frac{t^2}{2} \quad (3.215)$$

$$R(t) = R_0 + \left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0 - (\mu+\rho) R_0\right)t + \begin{bmatrix} \delta_1\left(r_2 I_0 - K_3 (R_2)_0\right) + \delta_2\left(r_2 I_0 - K_3 (R_2)_0\right) \\ -(\mu+\rho)\left(\delta_1 (R_1)_0 + \delta_2 (R_2)_0\right) \end{bmatrix} \frac{t^2}{2} \quad (3.216)$$

CHAPTER FOUR

4.0 RESULTS AND DISCUSSION

4.1 Variable and Parameter Values and Estimations

The parameter and variable values of six compartments model are assumed and estimated from the population of interest and also on Tuberculosis disease epidemiology. The description of the parameters of the model is show in the table below.

Table 4.1: Description of Parameter of the model 1 (yrs)

Parameters	Descriptions	Values	References
Λ	Recruitment rate	15 .00	Estimated
η	Case detection rate	0.570	Arthitian (2013)
r_1	Resistance to first line of treatment rate	0.400	Kumar Gupta et al (2018)
r_2	Resistance to second line of treatment rate	0.500	Kumar Gupta et al (2018)
δ_1	Recovery due to first line of treatment rate	0.800	Estimated
δ_2	Recovery due to second line of treatment rate	0.300	Estimated
ρ	Rate at which individual losses their immunity	0.400	Kumar Gupta et al (2018)

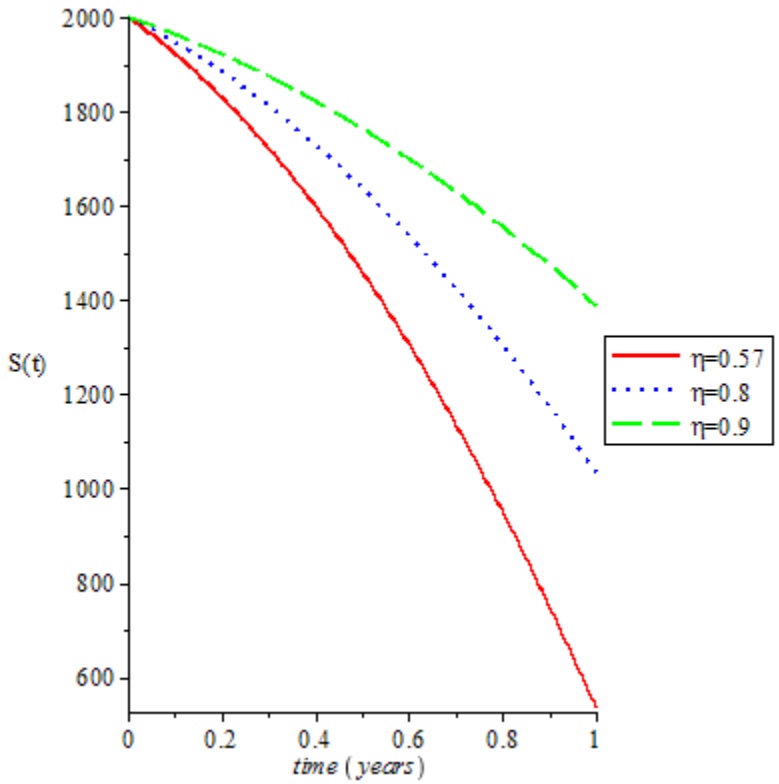

Figure 4.1: Show the Graph of susceptible Individuals against time for different case detection Rate η.

It was observed that the population of susceptible Individuals increases as case detection increases. This means that if the case detection is high more people will be in the class of susceptible individuals compare to when case detection rate is low.

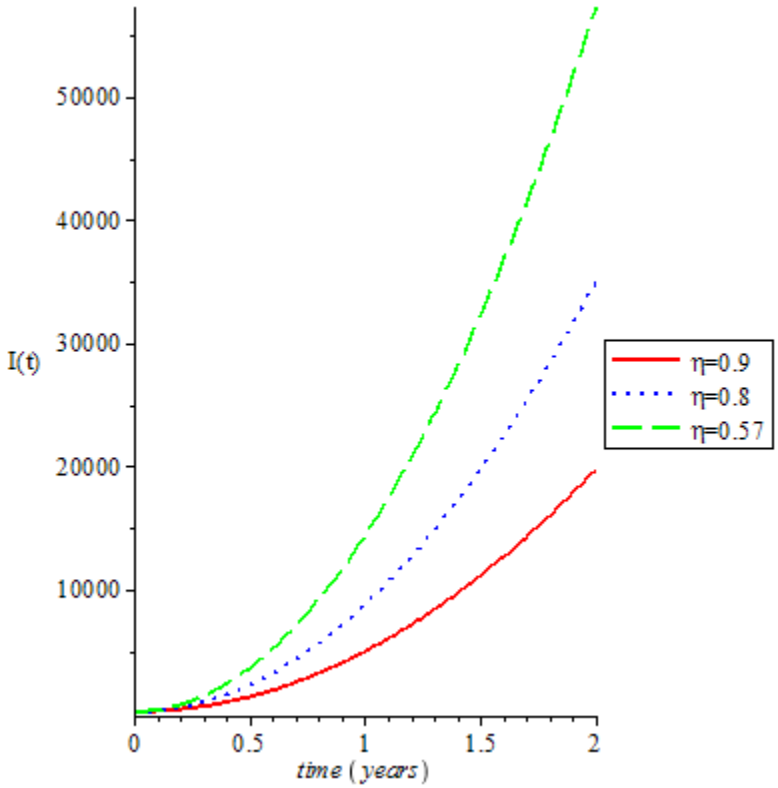

Figure 4.2: Show the Graph of Infected Individuals against time for different case detection Rate η.

It was observed that the population of infected individuals decreases as case detection rate increases. This means that if early case detection is high then fewer people will be infected compare to when the case detection rate is low as we will have high contact rate between the susceptible and infected individuals as a results of unidentified cases of Tuberculosis.

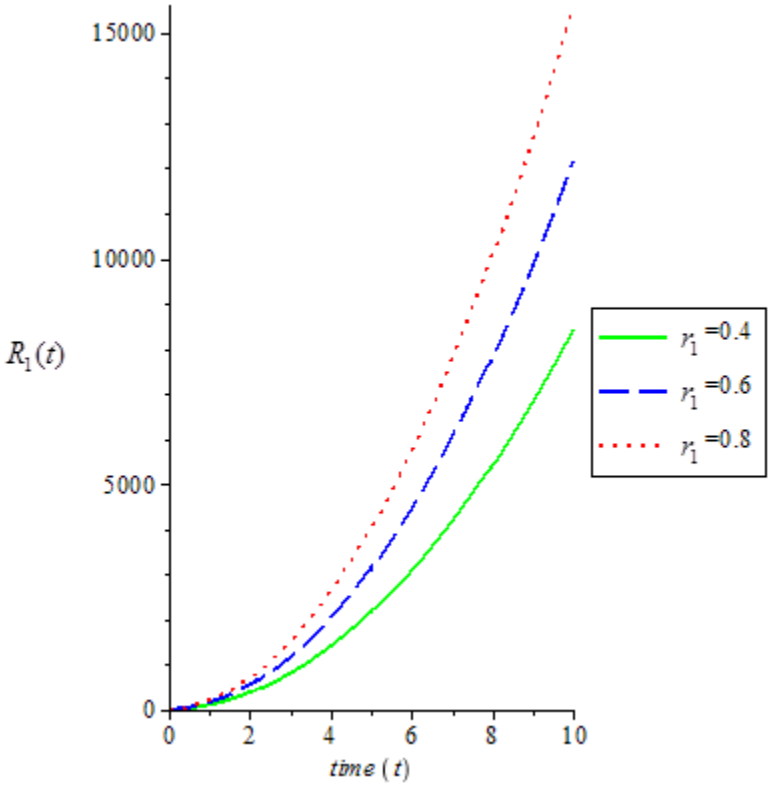

Figure 4.3: Show the Graph of Individuals who are resistance to first line of treatment against time for different resistance rate to first line of treatment r_1 .

We see from the graph that the population of resistant individuals increases as the resistance rate of first line of treatment increases. This shows that more people will move from infected class to resistance class of first line of treatment as resistance rate due to first line of treatment increases.

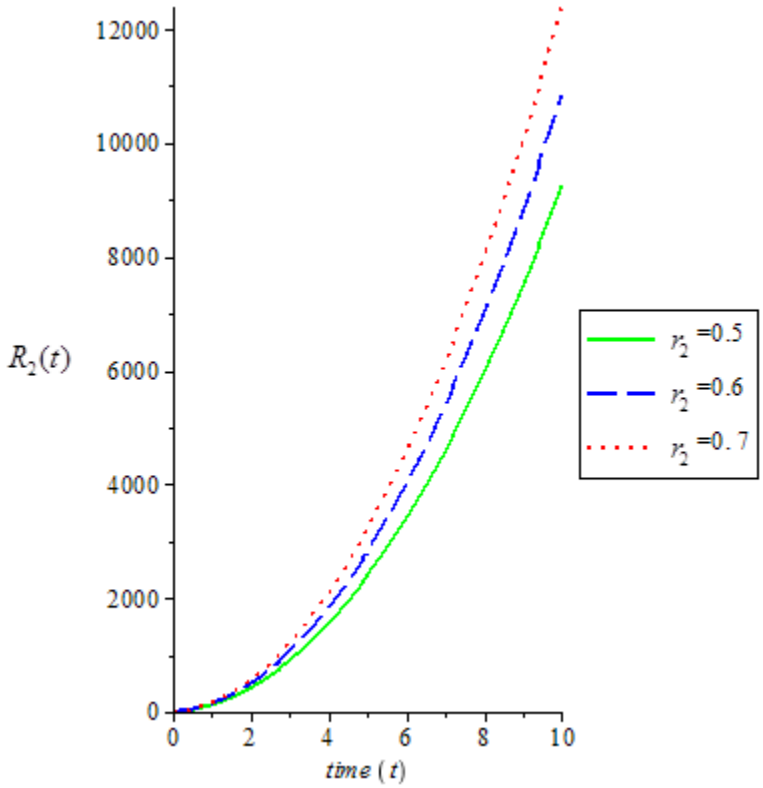

Figure 4.4: Show the Graph of Individuals who are resistance to second line of treatment against time for different resistance rate to second line of treatment r_2 .

We see from the graph that the population of resistant individuals of second line of treatment class increases as the resistance rate of second line of treatment increases. This shows that more people will move from resistance class of first line of treatment to resistance class of second line of treatment as resistance rate due to second line of treatment increases.

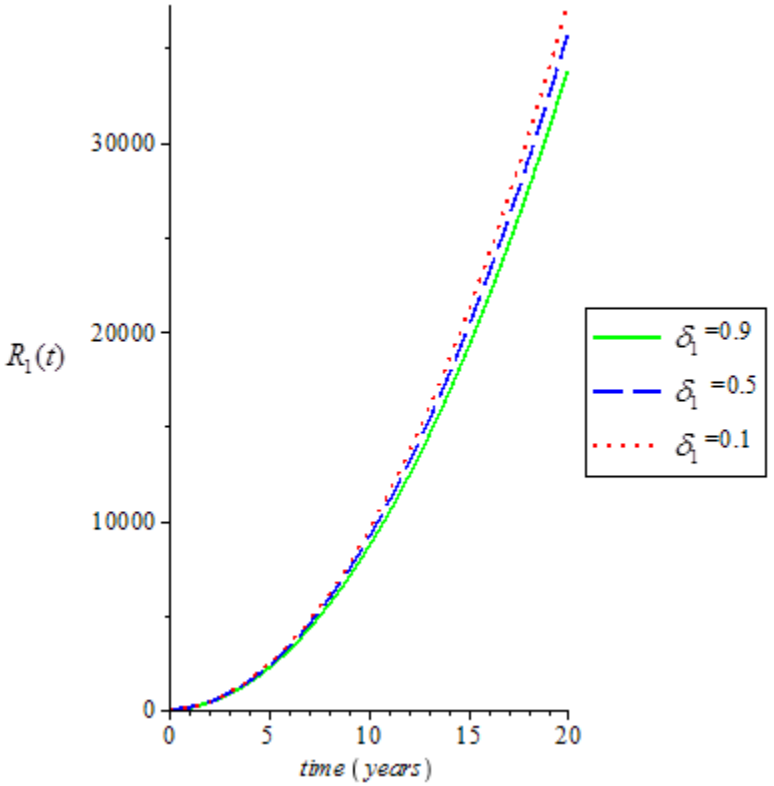

Figure 4.5: Show the Graph of Individuals who are resistance to first line of treatment against time for different recovery rate due to first line treatment δ_1.

We observed from the graph that the population of resistant individuals decreases as the recovery rate due to first line of treatment increases. This shows that more people will move from resistance class of first line of treatment to recovered class as recovery rate due to first line of treatment increases.

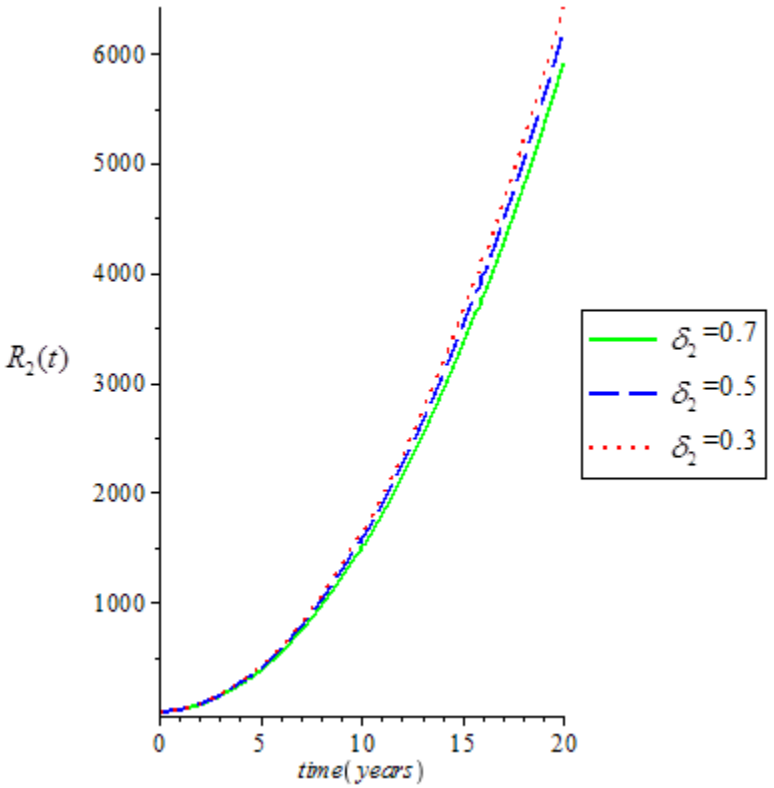

Figure 4.6: Show the Graph of Individuals who are resistance to second line of treatment against time for different recovery rate due to second line treatment δ_2.

We observed from the graph that the population of resistant individuals decreases as the recovery rate due to second line of treatment increases. This shows that more people will move from resistance class of second line of treatment to recovered class as recovery rate due to second line of treatment increases.

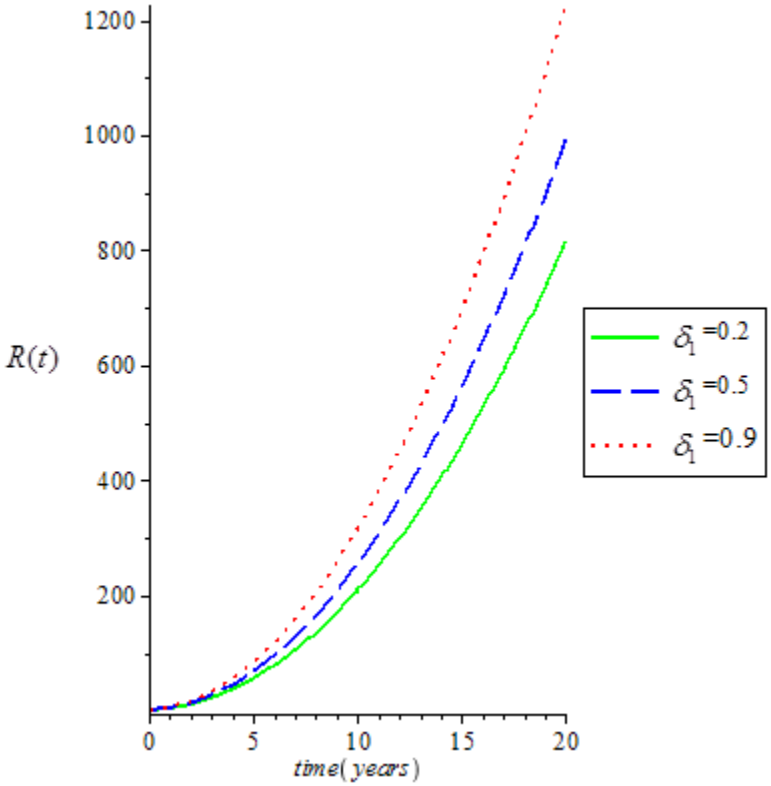

Figure 4.7: Show the Graph of Recovered Individuals against time for different recovery rate due to first line treatment δ_1.

It was noticed that the population of recovered class increases as the rate of recovery due to first line of treatment increases. This shows that more people will move to recovered class if adequate treatment is administered early.

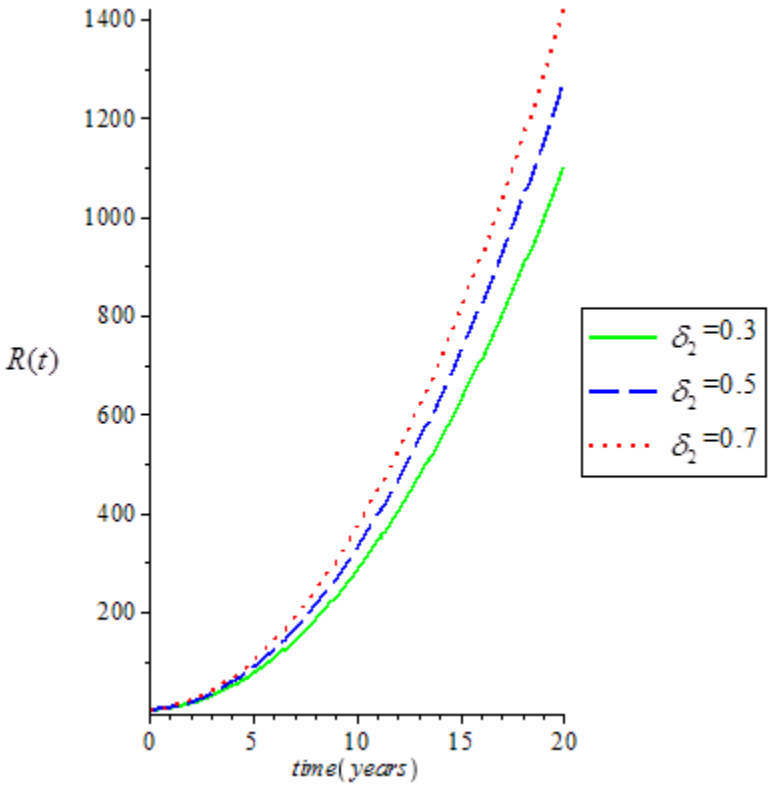

Figure 4.8: Show the Graph of Recovered Individuals against time for different recovery rate due to second line treatment δ_2 .

It was observed that the population of recovered class increases as the rate of recovery due to second line of treatment increases. This shows that more people will move to recovered class from Resistance class due to second line of treatment.

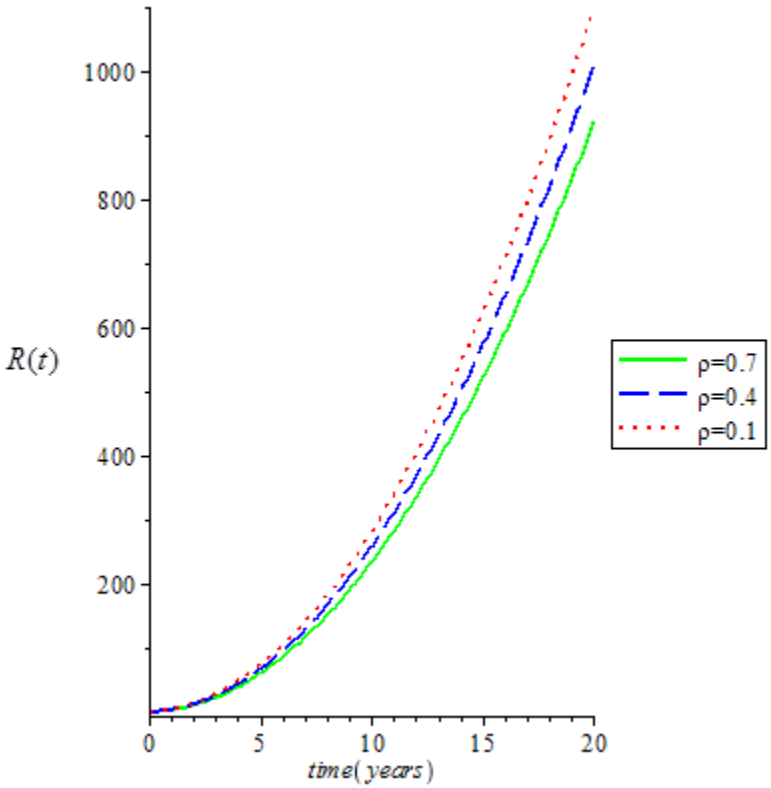

Figure 4.9: Show the Graph of Recovered Individuals against time for different Rate at which recovered individual loss their immunity ρ .

It was observed that the population of recovered class decreases as the Rate at which recovered individual loss their immunity increases. This shows that more people will move to susceptible class from Recovered class as they have contact with infectious individuals.

CHAPTER FIVE

5.0 CONCLUTION AND RECOMMENDATION

5.1 Summary and Conclusion

This study presents a deterministic model for the effects of case detection and Resistance to tuberculosis diseases. It is shown that the model is mathematically and epidemiologically meaningful in a feasible region. The positivity of the solution, equilibrium points, disease free and endemic equilibrium were carried out and analysed. The local and global stability of both local and endemic equilibrium points was analysed. The basic reproduction number using the next generation matrix was obtained. The analysis revealed that diseases free equilibrium is locally asymptotically stable if $R_0 < 1$ and globally stable if $R_0 \leq 1$. Also the disease endemic equilibrium point is asymptotically locally stable if $R_0 > 1$ and globally stable if $R_0 \geq 1$. Analytical solution using Homotopy Perturbation Method (HPM) were carried out with graphical results and interpretation of the model obtained.

From the results obtained in the model analysis, it was observed that when the case detection rate is high the infected population reduced drastically due to low contact rate between the susceptible population and infectious individuals. Also the result revealed that resistance population of first and second line of treatment increases as resistance rate of both classes increases respectively mainly due to treatment failure. The result further revealed that recovered class increases as recovery rate of first and second line of treatment increases and decreases as rate of loss of immunity increases due to high contact rate between the recovered individuals and infectious individuals.

5.2 Recommendation

Various studies and research are still going on to control and reduce the transmission of tuberculosis diseases. We hereby recommend that significant improvement on early case detection and sustained treatment strategy should be prioritized by the medical workers and other health organization in other to effectively control the spread and transmission of tuberculosis disease. We also recommend to researchers that want to model the dynamics of tuberculosis diseases transmission to focus more on effects of vaccination on the overall dynamic of the disease.

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