



ANALYSIS OF A MATHEMATICAL MODEL ON THE SPREAD AND CONTROL OF TUBERCULOSIS IN DENEBA TOWN, ETHIOPIA

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ABSTRACT: Most of mathematical modeling dealing disease curable by optimally: In this study, a non-linear deterministic model was developed to study the spread and control of Tuberculosis in the community of Deneba town in Ethiopia. The whole population of Deneba town were divided into five compartments namely, Susceptible class under fourteen, Susceptible class equal and above fourteen, Exposed class, Infected class and Recovered class was represented by S_1 , S_2 , E , I and R respectively. The basic reproduction number of the dynamical system R_0 is calculated by $R_0 = \frac{\beta_1 \delta \mu (\alpha + p \mu) + \beta_2 \delta c (\alpha + q \mu)}{\mu (\mu + c) (\alpha + \mu) (k + \mu + d)}$ which depends on ten parameters. And also the numerical value of the basic reproduction number based on the real data collected from Deneba town $R_0 = 2.981008273 > 1$. This in principle implies that the disease spreads in the community of Deneba town. Basically we found two equilibrium points namely disease free equilibrium point and endemic equilibrium point. As a result, the disease free equilibrium point is unstable and the endemic equilibrium point is stable. To control the spread of Tuberculosis, the basic reproduction number should be less than one. Therefore, this finding identify the control parameter β_2 is the contact rate of susceptible class equal and above fourteen with infected class, $\beta_2 = 0.068511865$ Thus, the basic reproduction number is less than one, the contact rate must be less than 0.068511865. The effect of the remaining control parameters was discussed in detail in the subsection.

KEY WORDS: Tuberculosis, Bacillus Calmette–Guerin, Reproduction Number, Numerical simulation. Equilibrium point

I. INTRODUCTION

Tuberculosis (TB) is an infectious air borne disease that has become a major global health problem. It is a bacterial disease caused by Mycobacterium and it typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB) [6, 7]. The genus Mycobacterium is divided in to two main groups: Mycobacterium tuberculosis complex and



environmental mycobacterium or non-tuberculosis mycobacterium. The Mycobacterium tuberculosis complex comprises the closely related species *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*, *Mycobacterium microti* and *Mycobacterium canettii* [14].

There are two types of TB; namely pulmonary tuberculosis and extra pulmonary tuberculosis. Pulmonary Tuberculosis (PTB) is any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. It may infect any part of the body, but most commonly occurs in the lungs [8]. Whereas, extra pulmonary Tuberculosis (EPTB) is tuberculosis of organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints, bones, and meninges [5]. It may coexist with pulmonary TB as well. In 15–20% of active cases, the infection spreads outside the respiratory organs, causing other kinds of TB [3]. Mycobacterium TB infection occurs through inhaling an aerosol droplet that is generated when patients with PTB cough, talk, sneeze, spit and sing. For *Mycobacterium bovis*, it can be transmitted through drinking of raw milk that may infect the tonsils presenting as scrofula (cervical lymphadenitis), or the intestinal tract, causing abdominal TB [12].

1.1 Epidemiology of tuberculosis in Ethiopia

Ethiopia is one of high TB endemic countries in the world. It ranks 13th in the list of 22 high burden countries, and 7th in Africa. The report also revealed that Ethiopia is among the 41 high TB/HIV co-infected countries in the world. The country had a high TB burden, high TB/HIV co-infection and had attempted to adapt and implement the Global plan to Stop TB for one decade 2006-2015 [14].

1.2 Clinical Manifestation of Tuberculosis

Once a person develops the disease PTB, there will be several suggestive clinical features, especially 2 weeks' or above duration of cough, sputum production and weight loss are important for the diagnosis of PTB [15]. The signs and symptoms of TB include fever, chills, night sweats, loss of appetite, unintentional weight loss and fatigue, coughing that lasts three or more weeks, coughing up blood, chest pain or pain with breathing or coughing and significant finger clubbing may also occur [1]. To control TB, the only currently available vaccine as of 2011 is Bacillus Calmette–Guerin (BCG),



while it is effective against disseminated disease in childhood, confers inconsistent protection against contracting pulmonary TB ^[9].

1.3 Risk factors of acquiring Tuberculosis

Age, gender, Socio-economic conditions and residence were risk factors one who acquire TB. From these risk factors, age is the main concern for this study. The risk of acquiring TB infection increases with age from infancy to early adult life, probably, because of increasing number and frequency of contacts ^[11]. TB is mainly a disease of adults in the age group of 15-64years. In addition prevalence of TB in children in the age group of 0-14 years is low due to that use of vaccine Bacille- Calmette-Guerin (BCG) decreases the risk of getting the infection by 20% and the risk of infection turning in to disease by nearly 60%. BCG is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated. However the immunity it induces decreases after about ten years ^[2].

1.4 Description of the study area

Deneba town is located in the North Shoa Zone, Amhara Region, Ethiopia. It is 98 kilometers away from the capital city of Addis Ababa. The town has latitude of 8°55'0" N and longitude of 41°40'0" E with an elevation of 2,680 meters. The number of total population size is 72,542 out of these 32,831(45.3%) are female and 39,741(54.7%) are males

1.5 Statement of the research Problem

Tuberculosis continues to cause a serious health problem in world-wide and it continues to claim lives in Ethiopia despite the interventions of government and private bodies. Hence there is an urgent need to assess the control strategies ^[13]. In this study, the following research questions had raised:

- ❖ What is the basic reproduction number?
- ❖ What are the control parameters in the spread and control of Tuberculosis?
- ❖ Which age group is more exposed to the dynamics of Tuberculosis?

Therefore, the present study was focused on the analysis of a mathematical model on the spread and control of tuberculosis in the case of Deneba town, Ethiopia.



1.6 Objectives of the study

1.6.1 General objective

The general objective of this study is analyzing a mathematical model on the spread and control of Tuberculosis in the case of Deneba town.

1.6.2 Specific objectives

The specific objectives of this study were;

- To develop a mathematical model on the dynamics of Tuberculosis disease.
- To determine the basic reproduction number of Tuberculosis.
- To investigate stability analysis of the equilibrium point.
- To identify the control parameters in the spread and control of TB.

II. METHODOLOGY

This study was used a non-linear deterministic model and the model is formulated by using system of ordinary differential equations. Qualitative analysis that is the stability analysis of the equilibrium point conducted and the result is included. The analysis can be done by classifying their equilibrium points as disease free equilibrium point and endemic equilibrium point. We can define a few theorems that are our methods are relevant to the thesis. The next generation matrix used to determining the reproduction number.

Basic definitions needed for the study they are following

2.2 Differential equation: is a mathematical equation for an unknown function of one or several variables that relates the values of the function itself and its derivatives of various orders.

2.3 Equilibrium point

For an autonomous system of ordinary differential equations $\frac{d\vec{y}}{dx} = \vec{f}(\vec{y})$ where, $\vec{y} = \begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{pmatrix}$

and $\vec{f} = \begin{pmatrix} f_1 \\ f_2 \\ \vdots \\ f_n \end{pmatrix}$ we refer to any point \vec{y}_* which satisfies $\vec{f}(\vec{y}_*) = \vec{0}$ is an equilibrium point.



2.4 Routh – Hurwitz Stability Criterion

Routh-Hurwitz stability Criterion helps us to determine the stability of the equilibrium point of a linear system by determining the location of the roots in the complex plane without finding the roots explicitly. Let us consider n-dimensional dynamical system together with $n \times n$ dimensional Jacobean matrix and the corresponding characteristic polynomial is given by

$$p_n(\lambda) = a_n \lambda^n + a_{n-1} \lambda^{n-1} + a_{n-2} \lambda^{n-2} \dots \dots \dots + a_1 \lambda + a_0$$
 Where, a_n, a_{n-1}, \dots, a_0 are coefficients of the characteristic polynomial and let the dynamical system has an equilibrium point $x_* = (x_1, x_2, \dots, x_n)$.

Necessary condition of stability: all the coefficients of the characteristic equation should be real and all the coefficients of the characteristic equation should be non zero.

Routh Hurwitz Stability Criterion is based on ordering the coefficients of the characteristic equation into an array, also known as Routh-Hurwitz Array.

Now the Routh- Hurwitz Array can be given by

$$\begin{array}{l|cccc} \lambda^n & a_n & a_{n-2} & a_{n-4} & a_{n-6} & \dots \\ \lambda^{n-1} & a_{n-1} & a_{n-3} & a_{n-5} & \dots & \dots \\ \lambda^{n-2} & b_1 & b_2 & b_3 & \dots & \dots \\ \lambda^{n-3} & c_1 & c_2 & c_3 & \dots & \dots \\ \cdot & d_1 & d_2 & d_3 & \dots & \dots \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \lambda^0 & \cdot & \cdot & \cdot & \cdot & \cdot \end{array}$$

Where, $b_1 = \frac{-1}{a_{n-1}} \begin{vmatrix} a_n & a_{n-2} \\ a_{n-1} & a_{n-3} \end{vmatrix} = \frac{-1}{a_{n-1}} (a_n a_{n-3} - a_{n-1} a_{n-2})$

$b_2 = \frac{-1}{a_{n-1}} \begin{vmatrix} a_n & a_{n-4} \\ a_{n-1} & a_{n-5} \end{vmatrix} = \frac{-1}{a_{n-1}} (a_n a_{n-5} - a_{n-1} a_{n-4})$

$b_3 = \frac{-1}{a_{n-1}} \begin{vmatrix} a_n & a_{n-6} \\ a_{n-1} & a_{n-7} \end{vmatrix} = \frac{-1}{a_{n-1}} (a_n a_{n-7} - a_{n-1} a_{n-6}) \dots \dots \dots$

Sufficient condition for stability: In the Routh-Hurwitz array if all elements in the first column are the same in sign then this implies that all eigenvalues are negative and then we can say that the equilibrium point is stable, unless it is unstable

2.5 Basic reproduction number

The basic reproduction number is denoted by R_0 , is the expected number of secondary cases produced in a completely susceptible population by a typical infective individual.



If $R_0 < 1$, then on average an infected individual produces less than one new infected individual over the course of its infectious period, and the infection cannot grow. Conversely, if $R_0 > 1$ then each infected individual produces on average more than one new infection and the disease can invade the population

III. COMPARTMENTAL MODEL IN EPIDEMIOLOGY

This work interested to study one of the basic epidemiological models of the deterministic models, also known as compartmental models, attempt to describe and explain what happens on the average at the population scale. These models categorize individuals into different compartments or subgroups^[10]. In this study compartmental model, an individual divided into five groups, namely Susceptible class under fourteen (S_1), Susceptible class equal and above fourteen (S_2), Exposed class (E), Infected class (I) and Recovered class (R).

3.1 The initial model

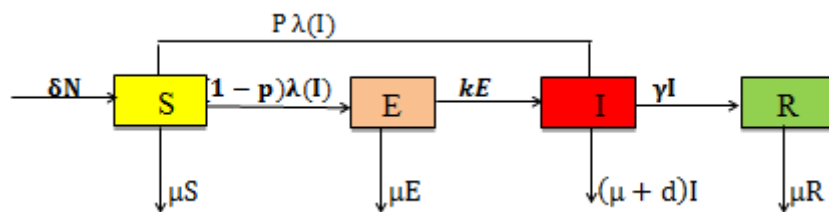


Fig 1: Flow chart of initial model

3.2 The extended mathematical model

To explore the role of age on the infection pattern between susceptible and infectious classes, the susceptible class was further divided into two age groups.

- Susceptible class under fourteen (S_1) years of age: who are healthy individuals under the age of fourteen but they can catch by the disease and
- Susceptible class equal and above fourteen (S_2) years of age: who are healthy individuals equal and above fourteen years of age but they can catch by the disease.
- The population under this study is divided in to five compartments.
- The population under study is heterogeneous.
- There is an age conversion rate from susceptible class under fourteen to susceptible class equal and above fourteen years of age.



- The susceptible class under fourteen directly moves to the infected class as a result of co-infection of TB with other related disease like HIV/AIDS by the proportion p and the remaining is exposed to TB by the proportion of $(1 - p)$ when individuals highly immunized.
- The susceptible class equal and above fourteen directly moves to the infected class as a result of co-infection of TB with other related disease like HIV/AIDS by the proportion q and the remaining is exposed to TB by the proportion of $(1 - q)$ when individuals highly immunized.
- The rate of natural death is the same for all compartments.
- All the parameters are positive.

Compartments, Parameters and their descriptions of the extended model as shown in the following table

Table 1: Compartments, Parameters the extended model

Compartments	Parameters	Description
$S_1(t)$		Susceptible class under fourteen years of age
$S_2(t)$		Susceptible class equal and above fourteen years of age
$E(t)$		Exposed class
$I(t)$		Infected class
$R(t)$		Recovered class
$N(t)$		Total population
	δ	The new born rate
	c	The age conversion rate from S_1 to S_2
	β_1	The contact rate of Susceptible class under fourteen with infected
	β_2	The contact rate of Susceptible class equal and above fourteen with infected
	p	The proportion of fast developing infectious of susceptible class under fourteen
	$1 - p$	The proportion of slow progression to TB of susceptible class under fourteen
	q	The proportion of fast developing infectious of S_2
	$1 - q$	the proportion of slow developing infectious of S_2
	α	Infectious rate
	k	Recovery rate
	μ	Natural death rate
	d	Disease induced death rate



Based on the above assumption the schematic diagram of the extended model represented as

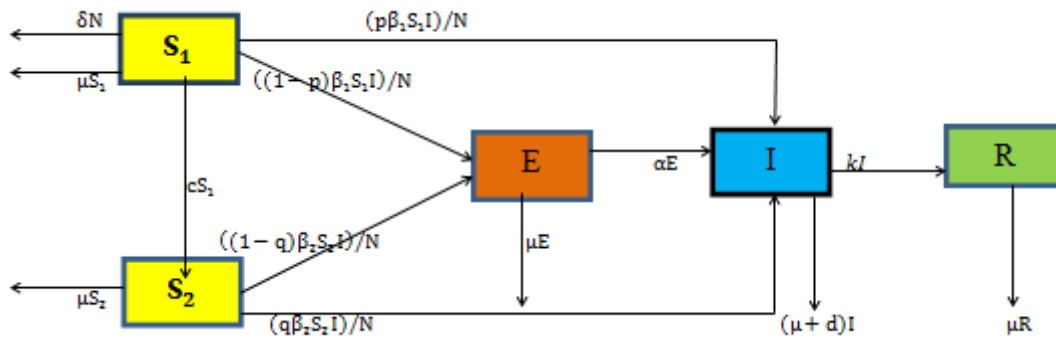


Fig 2: Schematic Diagram for Extended model

The corresponding dynamical systems are:

$$\frac{dS_1(t)}{dt} = \delta N(t) - (\mu + c)S_1(t) - \frac{\beta_1 S_1(t)I(t)}{N(t)} \quad (1)$$

$$\frac{dS_2(t)}{dt} = cS_1(t) - \mu S_2(t) - \frac{\beta_2 S_2(t)I(t)}{N(t)} \quad (2)$$

$$\frac{dE(t)}{dt} = \frac{(1-p)\beta_1 S_1(t)I(t)}{N(t)} + \frac{(1-q)\beta_2 S_2(t)I(t)}{N(t)} - (\alpha + \mu)E(t) \quad (3)$$

$$\frac{dI(t)}{dt} = \alpha E(t) + \frac{p\beta_1 S_1(t)I(t)}{N(t)} + \frac{q\beta_2 S_2(t)I(t)}{N(t)} - (k + \mu + d)I(t) \quad (4)$$

$$\frac{dR(t)}{dt} = kI(t) - \mu R(t) \quad (5)$$

With initial conditions:

$$S_1(0) = S_{1_0} \geq 0, S_2(0) = S_{2_0} \geq 0, E(0) = E_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0$$

And

The parameters $\delta, c, \beta_1, \beta_2, p, (1-p), q, (1-q), \alpha, k, \mu, d \geq 0$

3.3 Mathematical analysis of the model

This study discussed the mathematical analysis of the model to study positivity and boundedness of the solution, to determine basic reproduction number, to study equilibrium points and their stability analysis. Therefore, we set the proportion by introduce the new variables $s_1(t), s_2(t), e(t), i(t), r(t)$ and by

considering

$$S_1(t) = s_1(t)N(t), S_2(t) = s_2(t)N(t), E(t) = e(t)N(t), I(t) = i(t)N(t), R(t) = r(t)N(t).$$

Replacing the new variables in to (1) – (5) then the new dynamical system becomes:

$$\frac{ds_1}{dt} = \delta - (\mu + c)s_1 - \beta_1 s_1 i \quad (6)$$



$$\frac{ds_2}{dt} = cs_1 - \mu s_2 - \beta_2 s_2 i \quad (7)$$

$$\frac{de}{dt} = (1-p)\beta_1 s_1 i + (1-q)\beta_2 s_2 i - (\alpha + \mu)e \quad (8)$$

$$\frac{di}{dt} = \alpha e + p\beta_1 s_1 i + q\beta_2 s_2 i - (k + \mu + d)i \quad (9)$$

$$\frac{dr}{dt} = ki - \mu r \quad (10)$$

3.4 Positivity of the solution

The model equations (6) to (10) are to be epidemiologically meaningful and we need to prove that all the state variables are non-negative.

Theorem:

If $s_1(0) \geq 0$, $s_2(0) \geq 0$, $e(0) \geq 0$, $i(0) \geq 0$ and $r(0) \geq 0$ then the solution $s_1(t)$, $s_2(t)$, $e(t)$, $i(t)$, $r(t)$ of the system of equations (6) to (10) is always non-negative for $t \geq 0$.

Proof:

From equation (6) we have the dynamical system

$$\frac{ds_1(t)}{dt} = \delta - (\mu + c)s_1(t) - \beta_1 s_1(t)i(t)$$

And its solution is given by:

$$s_1(t) = e^{-[\beta_1(x(t)-x(0))+\mu t+ct]} \left[s_1(0) + \int_0^t \delta e^{\beta_1(x(s)-x(0))+\mu s+cs} ds \right]$$

It is clear from the solution that $s_1(t)$ is positive since $s_1(0) \geq 0$, $\delta \geq 0$ and exponential function always positive.

Secondly, from equation (7) we have the dynamical system

$$\frac{ds_2(t)}{dt} = cs(t) - \mu s_2(t) - \beta_2 s_2(t)i(t) \text{ And its solution is given by:}$$

$$s_2(t) = e^{-[\beta_2(y(t)-y(0))+\mu t]} \left[s_2(0) + \int_0^t cs_1(s) e^{\beta_2(y(s)-y(0))+\mu s} ds \right]. \text{ It is clear from the solution}$$

that $s_2(t)$ is positive since $s_2(0) \geq 0$, $s_1(t) \geq 0$, $c \geq 0$ and exponential function always positive.

Thirdly, from equation (8) we have the dynamical system

$$\frac{de(t)}{dt} = (1-p)\beta_1 s_1(t)i(t) + (1-q)\beta_2 s_2(t)i(t) - (\alpha + \mu)e(t) \text{ And its solution is given by:}$$

$$e(t) = e^{-(\alpha+\mu)t} \left[e(0) + \int_0^t e^{(\alpha+\mu)s} [(1-p)\beta_1 s_1(s)i(s) + (1-q)\beta_2 s_2(s)i(s)] ds \right]$$



From this solution we have seen that $e(t)$ is non-negative. Since $e(0), s_1(t), s_2(t), i(t) \geq 0$ and $\beta_1, \beta_2, (1-p), (1-q) \geq 0$ and also exponential function is always positive.

Fourthly, from equation (9) we have the dynamical system

$$\frac{di(t)}{dt} = \alpha e(t) + p\beta_1 s_1(t)i(t) + q\beta_2 s_2(t)i(t) - (k + \mu + d)i(t) \text{ and its solution is given by:}$$

$$i(t) = e^{-[(k+\mu+d)t - p\beta_1(z(t)-z(0)) - q\beta_2(w(t)-w(0))]} [i(0) + \int_0^t e^{(k+\mu+d)s - p\beta_1(z(s)-z(0)) - q\beta_2(w(s)-w(0))} \alpha e(s) ds]$$

It is clear from the solution that $i(t)$ is positive since $i(0) \geq 0, e(t) \geq 0, \alpha \geq 0$ and exponential function always positive.

Finally, from equation (10) we have the dynamical system

$$\frac{dr(t)}{dt} = ki(t) - \mu r(t), \text{ and its solution is given by: } r(t) = e^{-\mu t} \left[r(0) + \int_0^t ki(s)e^{\mu s} ds \right].$$

It is clear from the solution that $r(t)$ is positive since $r(0) \geq 0, i(t) \geq 0, k \geq 0$ and exponential function always positive.

3.5 Boundedness of the solution

Since, $N(t) = s_1(t) + s_2(t) + e(t) + i(t) + r(t)$ and differentiate $N(t)$ with respect to time t and substitute the corresponding values from the dynamical system (6) to (10) we get:

$$\frac{dN(t)}{dt} = \frac{ds_1(t)}{dt} + \frac{ds_2(t)}{dt} + \frac{de(t)}{dt} + \frac{di(t)}{dt} + \frac{dr(t)}{dt} = \delta - \mu N - di$$

$$\frac{dN}{dt} = \delta - \mu N - di \leq \delta - \mu N \Rightarrow N \leq \frac{\delta - e^{-\mu(t+c)}}{\mu}, \text{ It observed that as time } t \rightarrow \infty \text{ the total}$$

population $N(t) \leq \frac{\delta}{\mu}$ and we know that $N(t) > 0$. Equivalently it implies that $0 < N \leq \frac{\delta}{\mu}$

as $t \rightarrow \infty$. Therefore, the solutions of system of equation are bounded. The region $\Omega \subseteq \mathbb{R}_+^5$ is

$$\text{defined as: } \Omega = \left\{ s_1(t), s_2(t), e(t), i(t), r(t) \subseteq \mathbb{R}_+^5; 0 < N \leq \frac{\delta}{\mu} \right\}$$

3.6 Equilibrium points and their stability analysis

3.6.1 Disease free equilibrium point: are steady-state solutions where there is no tuberculosis disease. This is obtained by setting the right hand side of the model equation equal to zero. The disease free equilibrium point is

$$E_0 = (s_1, s_2, e, i, r) = \left(\frac{\delta}{\mu+c}, \frac{\delta c}{\mu(\mu+c)}, 0, 0, 0 \right)$$

3.6.2 Endemic equilibrium point



Endemic equilibrium point is a steady-state solution, where the disease persists in the population. The endemic equilibrium point can be expressed in terms of the reproduction number R_0 .

$$s_1^* = \frac{\delta}{\mu + c + \frac{\beta_1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]}$$

$$s_2^* = \frac{\left(\frac{c\delta}{\mu + c + \frac{\beta_1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]} \right)}{\mu + \frac{\beta_2}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]}$$

$$e^* = \frac{1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]$$

$$\left[\frac{\left(\frac{(1-p)\beta_1\delta}{\mu + c + \frac{\beta_1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]} \right)}{(\alpha + \mu)} + \frac{(1-q)\beta_2}{(\alpha + \mu)} \left[\frac{\left(\frac{c\delta}{\mu + c + \frac{\beta_1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]} \right)}{\mu + \frac{\beta_2}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]} \right] \right]$$

$$i^* = \frac{1}{2} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]$$

$$r^* = \frac{k}{2\mu} [(m-n) + \sqrt{(n-m)^2 + h(R_0-1)}]$$

$$\text{Where, } m = \frac{\delta(\alpha + p\mu)}{(\alpha + \mu)(k + \mu + d)} \text{ and } n = \frac{\beta_1\mu + \beta_2(\mu + c)}{\beta_1\beta_2}$$

3.6.3 Basic reproduction number

The basic reproduction number R_0 of the dynamical system (6) to (10) by using the next generation matrix method is $R_0 = \frac{\beta_1\delta\mu(\alpha + p\mu) + \beta_2\delta c(\alpha + q\mu)}{\mu(\mu + c)(\alpha + \mu)(k + \mu + d)}$.

1) 3.6.4 Stability analysis of disease free equilibrium point

The stability of the equilibrium point analyzed by linearizing the system of differential equations (6) to (10) to give the Jacobean matrix as the following manners:

$$f_1(s_1, s_2, e, i, r) = \delta - (\mu + c)s_1 - \beta_1 s_1 i$$

$$f_2(s_1, s_2, e, i, r) = cs_1 - \mu s_2 - \beta_2 s_2 i$$

$$f_3(s_1, s_2, e, i, r) = (1-p)\beta_1 s_1 i + (1-q)\beta_2 s_2 i - (\alpha + \mu)e$$

$$f_4(s_1, s_2, e, i, r) = \alpha e + p\beta_1 s_1 i + q\beta_2 s_2 i - (k + \mu + d)i$$

$$f_5(s_1, s_2, e, i, r) = ki - \mu r$$



The Jacobean matrix of the dynamical system is given by

$$J = \begin{bmatrix} -(\mu + c + \beta_1 i) & 0 & 0 & -\beta_1 s_1 & 0 \\ c & -(\mu + \beta_2 i) & 0 & -\beta_2 s_2 & 0 \\ (1-p)\beta_1 i & (1-q)\beta_2 i & -(\alpha + \mu) & (1-p)\beta_1 s_1 + (1-q)\beta_2 s_2 & 0 \\ p\beta_1 i & q\beta_2 i & \alpha & p\beta_1 s_1 + q\beta_2 s_2 - (k + \mu + d) & 0 \\ 0 & 0 & 0 & k & -\mu \end{bmatrix}$$

Computing this at disease free equilibrium point $E_0 = (s_1, s_2, e, i, r) = \left(\frac{\delta}{\mu+c}, \frac{\delta c}{\mu(\mu+c)}, 0, 0, 0\right)$

with the characteristic equation $Q(\lambda)$ at disease free equilibrium point given

by $Q(\lambda) = \det(J(E_0) - \lambda I) = 0$, where I is 5X5 identity matrix and we get the equation
 $\Rightarrow (\mu + \lambda)^2 [\lambda^3 + (m + n - w)\lambda^2 + (mn - (m + n)w - \alpha u)\lambda + (-mnw - \alpha um)] = 0$

Where,

$$m = \mu + c, n = \alpha + \mu, u = \frac{(1-p)\beta_1 \delta}{\mu+c} + \frac{(1-q)\beta_2 \delta c}{\mu(\mu+c)} \text{ And } w = \frac{p\beta_1 \delta}{\mu+c} + \frac{q\beta_2 \delta c}{\mu(\mu+c)} - (k + \mu + d)$$

$$\Rightarrow \lambda_{1,2} = -\mu$$

Here, the first two eigenvalues have negative sign and the other eigenvalues can determine by using Routh-Hurwitz criterion. Here, we have a polynomial as a form of

$$a_3 \lambda^3 + a_2 \lambda^2 + a_1 \lambda^1 + a_0 \lambda^0 = 0 \text{ Where } a_3 = 1, a_2 = m + n - w,$$

$$a_1 = mn - (m + n)w - \alpha u \text{ and } a_0 = -mnw - \alpha um. \text{ For this the Routh-Hurwitz array}$$

can be given by:

$$\begin{array}{l|l} \lambda^3 & a_3 \quad a_1 \quad 0 \\ \lambda^2 & a_2 \quad a_0 \quad 0 \\ \lambda^1 & b_1 \quad 0 \\ \lambda^0 & c_1 \quad 0 \end{array}$$

$$\text{Where, } b_1 = \frac{-1}{a_2} \begin{vmatrix} a_3 & a_1 \\ a_2 & a_0 \end{vmatrix} = a_1 - \frac{a_0 a_3}{a_2} = mn - (m + n)w - \alpha u + \left(\frac{mnw + \alpha um}{m+n-w}\right)$$

$$c_1 = \frac{-1}{b_1} \begin{vmatrix} a_2 & a_0 \\ b_1 & 0 \end{vmatrix} = (\mu + c)(\mu + \alpha)(k + \mu + d) - \beta_1 \delta (\alpha + p\mu) - \frac{\beta_2 \delta c (\alpha + q\mu)}{\mu}$$

Now, By Routh-Hurwitz criteria we observe the sign of first column of the Routh- array

$$a_3 = 1 > 0 \text{ And the sign of } a_2, b_1 \text{ and } c_1 \text{ so that we state conditions:}$$

Case 1:

$$\text{If } a_2, b_1, c_1 > 0 \text{ that is } m + n > w, mn - (m + n)w - \alpha u + \left(\frac{mnw + \alpha um}{m+n-w}\right) > 0 \text{ and}$$

$$c_1 > 0 \Rightarrow \frac{\beta_1 \delta \mu (\alpha + p\mu) + q\beta_2 \delta c (\alpha + q\mu)}{\mu(\mu+c)(\alpha+\mu)(k+\mu+d)} < 1 \Rightarrow R_0 < 1, \text{ then the first column of the Routh-Hurwitz}$$

array has no sign change this means all eigenvalues have negative sign.



Therefore, the disease free equilibrium point is stable if $R_0 < 1$.

Case 2:

If either of a_2 or b_1 or c_1 has negative in sign that is $m + n < w$ or

$$mn - (m + n)w - \alpha u + \left(\frac{mnw + \alpha um}{m+n-w}\right) < 0 \text{ Or } c_1 < 0$$

$$\Rightarrow (\mu + c)(\mu + \alpha)(k + \mu + d) < \beta_1 \delta(\alpha + p\mu) + \frac{\beta_2 \delta c(\alpha + q\mu)}{\mu}$$

$$\Rightarrow \frac{\beta_1 \delta \mu(\alpha + p\mu) + q\beta_2 \delta c(\alpha + q\mu)}{\mu(\mu + c)(\alpha + \mu)(k + \mu + d)} > 1 \Rightarrow R_0 > 1, \text{ then the first column of the Routh-Hurwitz array}$$

has a sign change this means all eigenvalues have not negative sign.

Therefore, the disease free equilibrium point is unstable if $R_0 > 1$.

IV. REAL PARAMETER ESTIMATION AND NUMERICAL SIMULATION

This study analyzed a non-linear S_1S_2EIR mathematical model for the dynamics of Tuberculosis using the secondary data collected from Deneba town, Amhara region, Ethiopia. The number of total population of Deneba town is 72542 to study the spread and control of Tuberculosis in Deneba town.

4.1 Collection of secondary data

The required secondary real data were collected from Deneba town started from 2017 up to half of 2018 years and the population information was given as shown in the table - 2 below.

Table 2: Data collected from 2017 January to 2018 May

Description	Total
Number of Deneba town populations	72,542
Number of individuals under fourteen	28,678
Number of individuals equal and above fourteen	43,864

Table 3: The collected real data about total population

Number of individuals who have taken TB test	509
Number of individuals who are infected by TB	107
Number of individuals who died by TB	8
Number of individuals under fourteen years of age who are directly go on infected class	4
Number of individuals equal and above 14 years of age who are directly go on infected class	91



Table 3: The gathered data about the TB diseases

Classes of the initial populations	Symbols	Total number
Initial Susceptible class under fourteen	S_{1n}	28,673
Initial Susceptible class equal and above fourteen	S_{2n}	4,481
Initial Exposed class	E_0	39,246
Initial Infected class	I_0	107
Initial Recovered class	R_0	35
Initial total population	N_0	72,542

In table – 4, the following are calculated and listed below:

Number of initial population in each compartments of the model

$$N_0 = S_{01} + S_{02} + E_0 + I_0 + R_0 = 4,481 + 2,8673 + 39,246 + 107 + 35 = 72,542$$

The average incubation period of TB is approximately 6 weeks of being exposed [4]. Thus

$$\text{infectious rate is } \alpha = \frac{1}{\text{mean incubation period}} = \frac{1}{6 \text{ weeks}} = \frac{1}{42} \text{ per days} = 0.02380952$$

The expected duration of infectious is the inverse of the recovery rate. For TB the infectious or contagious period is 2 weeks until on drugs [4]. Hence the recovery rate is

$$k = \frac{1}{\text{mean infectious period}} = \frac{1}{2 \text{ weeks}} = \frac{1}{14} \text{ per days} = 0.07142857$$

Let us describe the estimated parameters in the table form as follows



Table 5: The table contains the calculated parameters

Descriptions	Symbols	Corresponding formulas	Corresponding values
Infectious rate	α	$\frac{1}{\text{mean incubation period}}$	0.02380952
Recovery rate	k	$\frac{1}{\text{mean infectious period}}$	0.07142857
contact rate of S_1 with I	β_1	$\frac{\text{number of TB infectious individuals out of } S_1}{\text{number of individual who took TB test}}$	0.005893910
contact rate of S_2 with I	β_2	$\frac{\text{number of TB infectious individuals out of } S_2}{\text{number of individual who took TB test}}$	0.204322200
Conversion rate	c	$\frac{ \text{number of } S_2 - \text{number of } S_1 }{\text{the sum of initial susceptible individuals}}$	0.729685709
New born rate	δ	$\frac{\text{number of new born babies from total population}}{\text{number of total population}}$	0.016459430
TB induced death rate	d	$\frac{\text{number of individuals who died out by TB case}}{\text{number of initial infectious individual}}$	0.074766355
Natural death rate	μ	$\frac{\text{no of individuals who died out by non TB case}}{\text{number of total population}}$	0.007044195
Proportion of fast developing infectious of S_1	p	$\frac{\text{Number of } S_1 \text{ individuals who are directly go to infectious class}}{\text{Total number of infected individuals}}$	0.037383178
Proportion of slow developing infectious of S_1	$1 - p$	$1 - p$	0.962616822
Proportion of fast developing infectious of S_2	q	$\frac{\text{Number of } S_2 \text{ individuals who are directly go to infectious class}}{\text{Total number of infected individuals}}$	0.850467290
Proportion of slow developing infectious of S_2	$1 - q$	$1 - q$	0.149532710



4.2 Basic reproduction number

$$R_0 = \frac{\beta_1 \delta \mu (\alpha + p \mu) + \beta_2 \delta c (\alpha + q \mu)}{\mu (\mu + c) (\alpha + \mu) (k + \mu + d)} = 2.981008273$$

Thus shows that $R_0 = 2.981008273 > 1$ hence, TB diseases spread in the community.

4.3 Equilibrium points and their stability analysis

The disease free equilibrium point is $E_0 = (0.022341200, 2.314253732, 0, 0, 0)$ and the disease free equilibrium point is unstable.

The endemic equilibrium point is

$$E^* = (s_1^*, s_2^*, e^*, i^*, r^*) = (0.022329001, 0.775986776, 0.052753258, 0.068286728, 0.692431616)$$

And the endemic equilibrium point is stable which means the disease exists and spread in the community.

4.4 Numerical simulation

In this study the basic reproduction number of a nonlinear $S_1 S_2 EIR$ mathematical model is

$$R_0 = \frac{\beta_1 \delta \mu (\alpha + p \mu) + \beta_2 \delta c (\alpha + q \mu)}{\mu (\mu + c) (\alpha + \mu) (k + \mu + d)}$$

This depends on ten parameters

1. Let us take the parameter β_1 and the remaining parameter is taken as constant then

$$R_0(\beta_1) = 0.113746587\beta_1 + 2.980356197$$

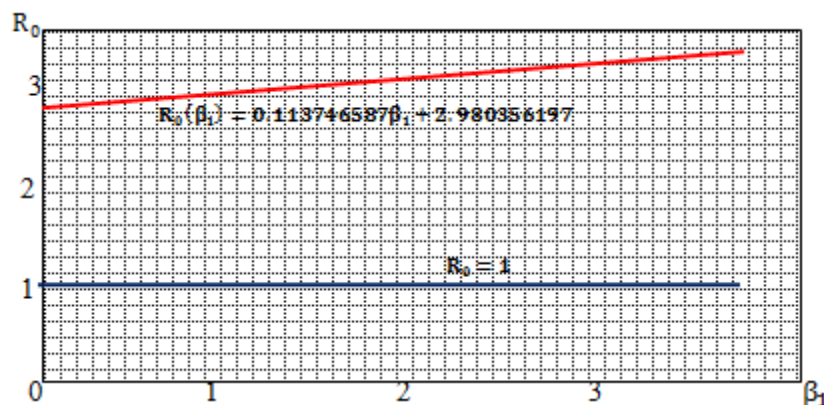


Figure3: R_0 versus β_1

From this graph, observe that there is no any intersection point between R_0 and β_1 in the first quadrant. Therefore the parameter β_1 is not our control parameter.



Let us take the parameter β_2 and the remaining parameter is taken as constant and the reproduction number in terms of β_2 is $R_0(\beta_2) = 14.58649432\beta_2 + 0.000652076$

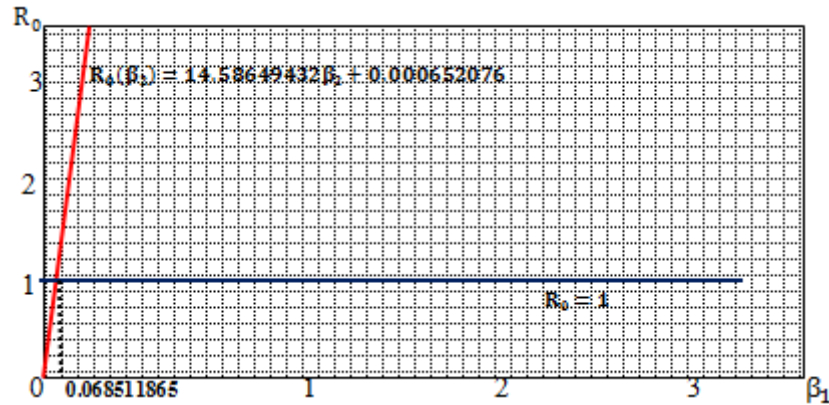


Figure 4: R_0 versus β_2

From this graph, observe that $R_0 < 1$ when $\beta_2 < 0.068511865$ and $R_0 > 1$ when $\beta_2 > 0.068511865$

- Let us take the parameter δ , and the remaining parameter is taken as constant and the reproduction number in terms of δ is: $R_0(\delta) = 181.1128781\delta$

In this following graph we used R_0 , units mention 100 and (δ) units mention 1 unit

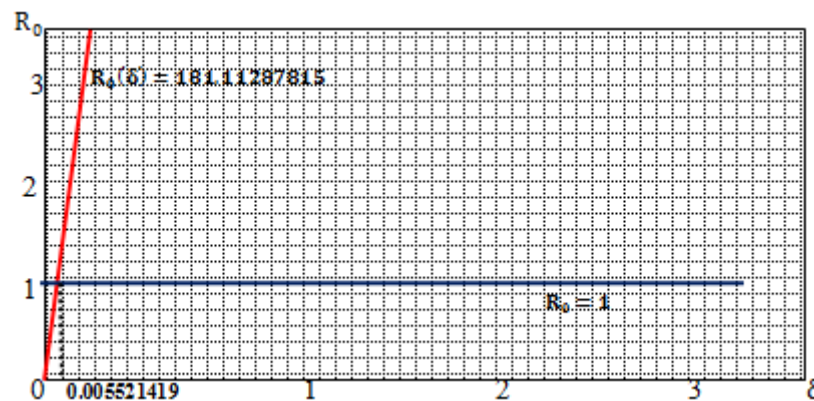


Figure 5: Basic reproduction number versus the new born rate

From this graph: $R_0 < 1$ when $\delta < 0.005521419$ and $R_0 > 1$ when $\delta > 0.005521419$

- Let us take the parameter α and the remaining parameter is taken as constant and the reproduction number in terms of α is: $R_0(\alpha) = \frac{0.002454636\alpha + 0.000014701}{0.000795260\alpha + 0.000005602}$

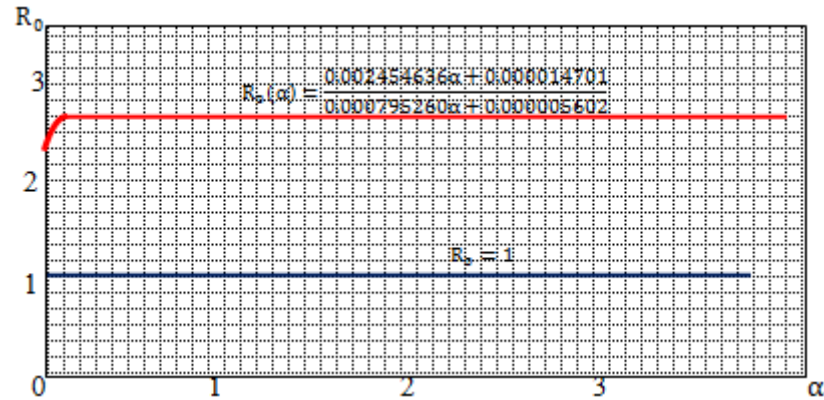


Figure 6: Basic reproduction number versus infection rate

From this graph, observe that there is no any intersection point between R_0 and α in the first quadrant. Here the parameter α is not our control parameter.

- Let us take the parameter p and the remaining parameter is taken as constant and the reproduction number in terms of p is $R_0(p) = 0.000196079p + 2.981018947$

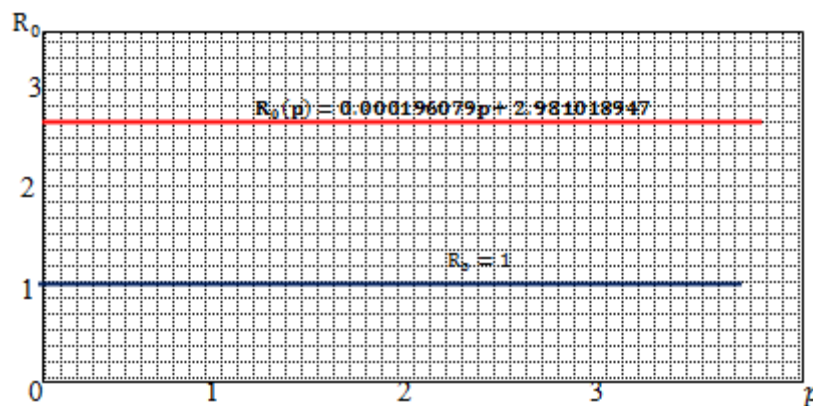


Figure 7: Basic reproduction number versus proportion of fast developing infection S_1

And the parameter p in terms of reproduction number is expressed as $p = \frac{R_0 - 2.981018947}{0.000196079}$.

Then the graphical representation of basic reproduction number versus the proportion of fast developing infection of S_1 and P as shown in figure – 6:

From this graph, observe that there is no any intersection point between R_0 and p in the first quadrant. Here, the Proportion of fast developing infectious of S_1 , p is not our control parameter.

- Let us take the parameter q and the remaining parameter is taken as constant and the reproduction number in terms of q is $R_0(q) = 0.704487101q + 2.381831520$

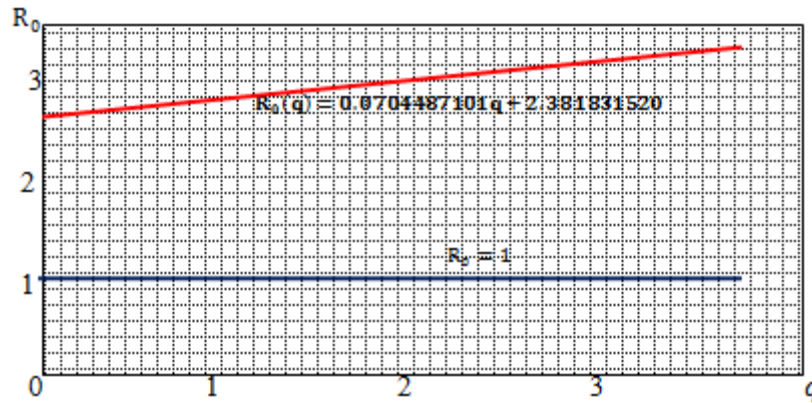


Figure 8: Basic reproduction number versus proportion of fast developing infectious of susceptible equal and above fourteen years

From this graph we observe that there is no any intersection point between R_0 and q in the first quadrant. Here, the Proportion of fast developing infectious of S_2 , q is not our control parameter.

- Let us take the parameter c is the age conversion rate and the remaining parameter is taken as constant and the reproduction number in terms of c is

$$R_0(c) = \frac{0.004442968c + 0.000000016}{0.000033305c + 0.000000235}$$

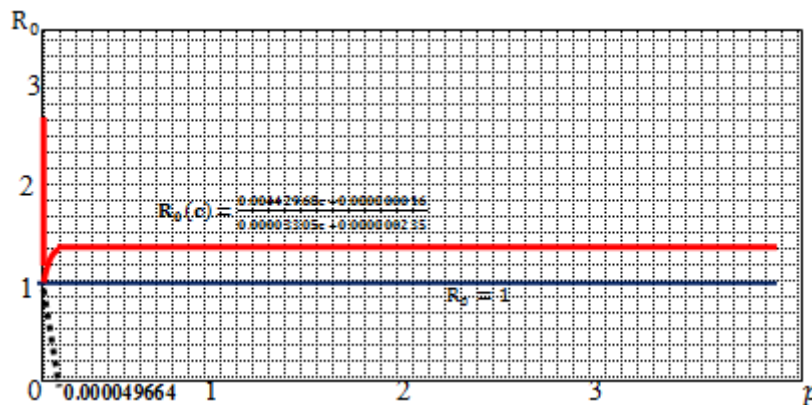


Figure 9: Basic reproduction number versus the age conversion rate

From this graph, observe that the point $(0.000049664, 1)$ is an intersection point of R_0 and c . and the reproduction number $R_0 < 1$ when $c < 0.000049664$ and $R_0 > 1$ when $c > 0.000049664$.

- Let us take the parameter k is the recovery rate and the remaining parameter is taken as constant and the reproduction number in terms of k is

$$R_0(k) = \frac{0.0000731e}{0.000160121k + 0.000013100}$$



Then the graphical representation of basic reproduction number versus the recovery rate k is:

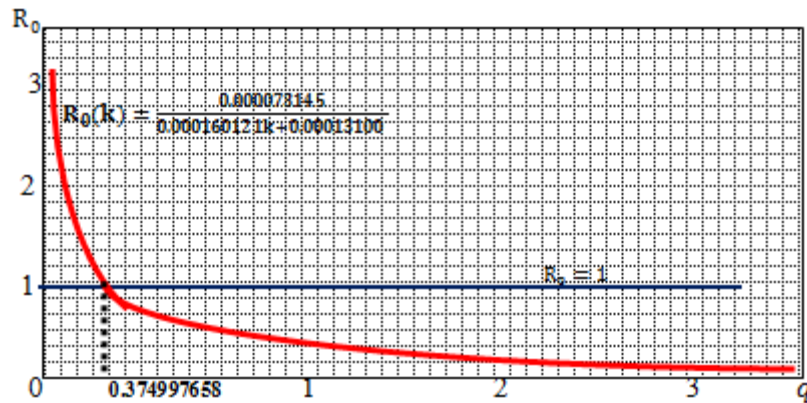


Figure 10: Basic reproduction number versus the recovery rate

From this graph, observe that the point $(0.374997658, 1)$ is an intersection point of R_0 and k and the reproduction number $R_0 < 1$ when $k > 0.374997658$ and $R_0 > 1$ when $k < 0.374997658$.

- Let us take the parameter d and the remaining parameter is taken as constant and

the reproduction number in terms of d is
$$R_0 = \frac{0.000073145}{0.000160121d + 0.000012565}$$
,

Then the graphical representation of basic reproduction number versus the TB induced death rate d is:

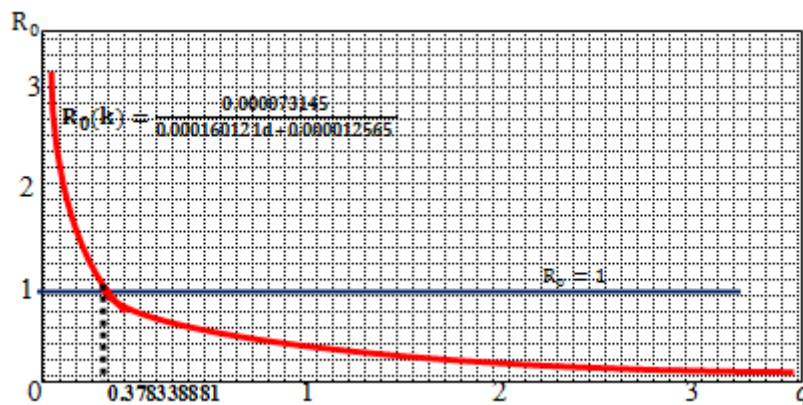


Figure 11: Basic reproduction number versus the TB induced death rate.

From this graph, observe that the point $(0.37833881, 1)$ is an intersection point of R_0 and d . And the reproduction number $R_0 < 1$ when $d > 0.37833881$ and $R_0 > 1$ when $d < 0.37833881$.



10. Let us take the parameter μ and the remaining parameter is taken as constant and the reproduction number in terms of μ is

$$R_0(\mu) = \frac{0.000003627\mu^2 + 0.002089317\mu + 0.000058427}{\mu(\mu^3 + 0.8996900154\mu^2 + 0.127530645\mu + 0.002539913)}$$

Then the graphical representation of basic reproduction number versus the natural death rate μ is

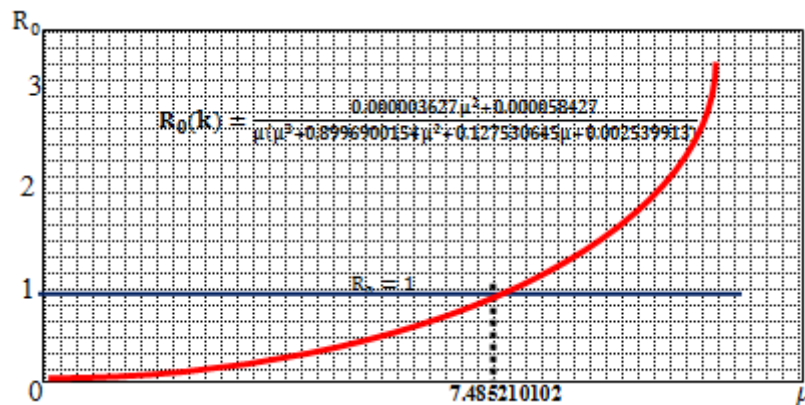


Figure 12: Basic reproduction number versus NATURAL death rate

From this graph, observe that the point $(7.485210102, 1)$ is an intersection point of R_0 and μ and the reproduction number $R_0 < 1$ when $\mu < 7.485210102$ and $R_0 > 1$ when $\mu > 7.485210102$.

V. RESULTS AND DISCUSSIONS

This study has considered non-linear dynamical system to study the dynamics of Tuberculosis disease at the population level. Basically, the basic reproduction number R_0 is $R_0 = \frac{\beta_1 \delta \mu (\alpha + p \mu) + \beta_2 \delta c (\alpha + q \mu)}{\mu (\mu + c) (\alpha + \mu) (k + \mu + d)}$ which depends on ten parameters and also the numerical value of the basic reproduction number based on the real data collected from Deneba town is $R_0 = 2.981008273 > 1$. This in principle implies that the disease spreads in the community of Deneba town. And also from the above graph, discuss about how basic reproduction number R_0 affected by the parameters change. Figure 4 shows that how R_0 affected by β_2 . If $\beta_2 > 0.068511865$ then $R_0 > 1$ and the disease spreads in the community and if $\beta_2 < 0.068511865$ then $R_0 < 1$ and also the disease is not spread in the community. Figure 5 shows that how R_0 affected by δ . If $\delta > 0.005521419$ then $R_0 > 1$ and also the disease spreads in the community. If $\delta < 0.005521419$ then $R_0 < 1$ and also the disease is not spread in the community.



Figure 9 shows that how R_0 affected by c . If $c > 0.000049664$ then $R_0 > 1$ and also the disease spreads in the community. If $c < 0.000049664$ then $R_0 < 1$ and also the disease is not spread in the community. Figure 10 shows that how R_0 affected by k . If $k < 0.374997658$ then $R_0 > 1$ and also the disease spreads in the community. If $k > 0.374997658$ then $R_0 < 1$ and also the disease is not spread in the community. Figure 11 shows that how R_0 affected by d . If $d < 0.378338881$ then $R_0 > 1$ and also the disease spreads in the community. If $d > 0.378338881$ then $R_0 < 1$ and also the disease is not spread in the community. Figure 12 shows that how basic reproduction number R_0 affected by the natural death rate μ . If $\mu > 7.475760102$ then $R_0 > 1$ and also the disease spreads in the community. If $\mu < 7.475760102$ then $R_0 < 1$ and also the disease is not spread in the community.

VI.

CONCLUSIONS,

RECOMMENDATIONS AND FUTURE WORK

Based on the real data collected from Deneba town, the numerical value of the basic reproduction number of this S_1S_2EIR mathematical model is $R_0 = 2.981008273 > 1$. This in principle implies that the disease spreads in the community of the study area.

Based on this finding, the following points will be recommended

- The contact rate of susceptible class equal and above fourteen with infected class β_2 should be less than **0.068511865**
- The recovery rate k should be greater than **0.374997658**

This study extend the model by considering age groups on the infection pattern between susceptible and infectious classes, by dividing the susceptible class into two age groups: Therefore, the next researchers will be considering the age groups in detail as by dividing the susceptible class into more than two age groups.

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