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Stability Analysis of Mathematical Model on the Dynamics of Tuberculosis

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Abstract
A new version of the mathematical model for the optimal control of tuberculosis, incorporating vaccination, public health campaigns, case detection, quarantine, and sanitarium as control strategies, is developed and studied. The basic properties of the model in terms of existence and uniqueness, positivity, and boundedness of the solution were established. The model has two equilibrium points, namely the disease-free and endemic equilibrium points. Also, the reproduction number of the model was computed by the next-generation matrix method. The disease-free equilibrium point of the model was established to be locally and globally asymptotically stable provided that the basic reproduction number is less than unity and unstable otherwise. Furthermore, using the common quadratic Lyapunov function in conjunction with the Lassalle invariance principle, the endemic equilibrium point of the model is established to be globally asymptotically stable.

Keywords: tuberculosis, reproduction number, sensitivity, management.

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by mycobacterium (tubercle bacillus). The disease spreads from one individual to another through air. Infected persons release droplets of Mycobacterium tuberculosis bacteria into the air by coughing, sneezing or spitting mucus containing the bacteria onto surfaces. This droplets or mucus contain large number of small respiratory droplets nuclei that evaporates and dispersed into the air almost instantly. These nuclei implant themselves in the lung when inhaled. In most cases, a competent immune system limits the multiplication of the tuberculosis bacilli, although some bacilli remain dormant but viable, rendering a condition known as Latent TB Infection (LTBI), (Center for Disease and control (CDC), 2000).

Basically, there are two types of TB, namely: Pulmonary TB which affects the lung (the commonest and infectious form of the disease) and Extra-pulmonary TB that affects organs such as pleura, lymph nodes, spine, joints, abdomen or genitourinary track.

Worldwide 8.6 million people fell ill due to TB, of which 1.3 million people die annually. In Africa, the TB incidences per 100,000 population is 262 while the prevalence is 293 as per World Health Organization (WHO), (2013). At global level, TB is the seventh most important cause of global premature mortality and disability and it is projected to remain among the ten leading causes of disease burden even in the year 2020 (Nyerere *et al*., (2014).

The use of mathematical modeling in the theory and practice of disease management and control have increase due to the fact that, the approach helps in figuring out control strategies and making decisions that are of significant importance to the control of the disease (Nyerere, *et al.,* 2014).

TB can be managed and control through the following: Public campaign to create awareness on preventive hygiene and avoiding crowding in a localized environment, vaccination, quarantine and sanitarium for preventing the progression from latent infection to active TB through, drug treatment. The management and control approach may include; Direct Observation Therapy Strategy (DOTS), routine – collected data, short course chemotherapy on TB, early identification, screening and isolation of infectious TB patients; effective engineering controls (environmental controls such as general ventilation, high –

efficiency particulate air [HEPA) filters, or Ultraviolet Germicidal Irradiation [UVGGI]); the adoption of appropriate respiratory protection (surgical masks and particulate respirators such as HEPA Masks); health – care worker TB training, education, counseling.

Mathematical models have played a key role in understanding and formulation of TB control strategies, which can be used in establishment of interim goals for intervention programs: Earlier models (prior to the 1970s) targeted the evaluation of control strategies. Such as vaccination strategies. However, these control strategies have not worked well towards the elimination of TB globally or even regionally. The reasons behind the lack of success of these control strategies are, either these strategies have not been applied by the policy – makers or they are not true control strategies Revelle, et al,. (1967). For instance, although 12% of GNP of the USA is spent on health care, the amount spent on prevention is very small. WHO estimated that if the amount of aid spent on TB treatment programmes could be increase from 15 to 100 million dollars yearly, then 1.2 million deaths could be avoided every year Murray, (1992). That is, the death toll would be reduce by over 30%. This leaves the far – fetching questions of what are the best strategies for the complete elimination of TB. Therefore, the focus should include control measures in the latent – TB class. The reason is that the huge pool of latent – TB patients is a time bomb or reservoir of infection (Reichaman & Tanne, 2002).

Lietman & Blower (2000) developed two vaccine models; pre-exposure and post exposure models. The susceptible and latent classes as divided into unvaccinated and vaccinated subclasses. Pre exposure vaccinations only vaccinate newborns and post exposure vaccinations only apply to the individuals with latent TB. A third sub-class of the latent TB class is added to represent the waned stage of vaccination for those with latent TB. They were able to identify distinct vaccination strategies for different nations that wish to eliminate TB. For developed countries, where prevalence of the latent TB is low, only a pre-exposure vaccine with treatment of active TB would be necessary. For developing nations, where the prevalence of latent TB is high, a combination of pre-exposure and post-exposure vaccine with treating active TB will be the most effective strategy. Emvudu & Tawa (2010) developed TB model with two differential infectivity and N latent classes. The classes are susceptible (S) latently infected with n strategies, exposed (E), infectious (I) have active TB, recovered (R) and lost sight (L) i.e. (the health personal does not know their epidemiological status) it was of SEILR type. On exposed and latent period through E …E_n stages, Emvudu & Tawa (2010) found that TB is globally asymptotically stable and possesses the only globally stable equilibrium state.

In this paper a deterministic sets of ordinary differential equations were developed taking into consideration of some control levels and the stability of the model equation were investigated.

Materials and Methods

The following are the main assumptions made in in formulating the model:

(i) All exposed individuals suspected of TB case are quarantined.
(ii) Treatment of infected individuals occur in the sanitarium.
(iii) Quarantined individuals who are tested positive will be taken to sanitarium for immediate treatment.
(iv) Screening is done to the exposed individual to detect infected individuals.
(v) Natural death occurs across the compartments.
(vi) All exposed individuals that are tested negative are going to the quarantine.
(vii) Recruitment rate into the susceptible population remain constant.
(viii) Those on vaccine become exposed on expiration of the vaccine efficacy.

Table 1: Definitions of variables of the model

Variable	Definition
S(t)	The population of susceptible individuals at time, t
V(t)	The population of vaccinated individuals at time t
E(t)	The population of exposed individuals at time, t
Q(t)	The population of individuals suspected with the symptoms of the disease at time, t
I(t)	The population of infected individuals at time, t
J(t)	The population of individuals in a sanitarium at time, t
R(t)	The population of recovered/treated individuals at time, t
N(t)	Total population at time, t

Table 2: Definitions of parameters of the model

Parameters	**Definition**
Λ	Birth Rate
μ	Natural mortality rate
ρ	Proportion of vaccination at birth
$1-p$	Proportion of those not vaccinated at birth
d_2	TB-induced death rate for individuals in the sanitarium
d_1	TB=induced death rate for infected individuals
ω	Proportion of quarantined individual that are infected and go for treatment
$1-\omega$	Proportion of quarantine individuals that are not infected
q	The rate at which susceptible individuals are vaccinated
α	The rate at which infected individuals move to sanitarium
β	Per capita TB transmission rate
θ	The rate at which new born are vaccinated
r_1	The recovery rate of individuals in the sanitarium
π	The efficacy of vaccine
λ	The force of infection
τ	Rate at which the quarantine individuals are diagnose
p	The rate of progression from expose to infected class
γ	Proportion of exposed individuals that are quarantined
$1-\gamma$	Proportion of exposed individuals that are not quarantined
η	Probability of acquiring TB infections per contact with an infectious individual

Description of the modified model

The total population at time t denoted by $N(t)$ is divided into seven mutual exclusive compartments (depending on the epidemiological status of individuals in the population). The compartments are; the population of susceptible individuals, $S(t)$, the population of vaccinated individuals, $V(t)$, the population of exposed individuals, $E(t)$, the population of quarantined individuals, $Q(t)$, the population of infected individuals, $I(t)$, the population of individuals under sanitarium $J(t)$, and the population of recovered individuals, $R(t)$. it is refer to a compartmental-based model as SVEQIJR model. Let the force of infection be given as $\lambda = \frac{\beta(I+\eta J)}{N}$, where the total population is given by:

$$N(t)=S(t)+E(t)+I(t)+Q(t)+J(t)+V(t)+R(t).$$

The population of susceptible individuals is generated by the proportion $(1-\rho)\Lambda$ i.e. new births

that were not vaccinated, vaccinated individuals who lose immunity at the rate θ and the proportion of quarantine individuals that are confirmed negative with TB given by $(1-\omega)\tau$. The susceptible population is reduced by natural death at the rate μ those that are vaccinated at the rate q and by those that become infected and move to the exposed compartment at the rate λ. Thus, the equation governing the dynamics of susceptible individuals is given by

$$\frac{dS}{dt} = (1-\rho)\Lambda + \theta V + (1-\omega)\tau Q - (\lambda + q + \mu)S.$$

The population of vaccinated individuals is generated by the proportion of those that are successfully vaccinated at birth given by ρΛ and the susceptible individuals that are vaccinated at the rate q. This population is reduced by those who lose immunity against TB at the rate θV. The vaccinated population further reduces due to the natural death at the rate μ. Hence, the equation governing the dynamics of the vaccinated population is as follows:

$$\frac{dV}{dt} = \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V.$$

The population of exposed individuals is generated by those susceptible and vaccinated individuals that are suspected with TB at the rates λ and $\lambda(1-\pi)$, respectively. This population decreases due to the progression into the infected class at the rate $p(1-\gamma)$, those that are quarantine at the rate $p\gamma$ and by the natural death at the rate μ. Hence,

$$\frac{dE}{dt} = (S + (1-\pi)V)\lambda - (p+\mu)E.$$

The population of quarantine individuals is generated by the proportion of those that are suspected with TB at the rate of γ. It reduces by those who move to the susceptible class after they are confirmed negative with TB at the rate $(1-\omega)\tau$, those that go for treatment at the rate $\omega\tau$ and the natural death at the rate μ. Thus, the equation:

$$\frac{dQ}{dt} = p\gamma E + \phi_1 - (\tau + \mu)Q.$$

The population of the infected individuals is generated by the proportion of those confirmed infected at the rate $p(1-\gamma)$ and reduced by TB-induced and natural deaths at the rates d_1 and μ, respectively. The population also reduces by αI, i.e. the proportion of those that go for treatment. Hence,

$$\frac{dI}{dt} = p(1-\gamma)E + \phi_2 - (\alpha + d_1 + \mu)I.$$

The population of individuals in the sanitarium compartment increases by proportion of those that go for treatment from the infected class at the rate α and from quarantine compartment at the rate $\omega\tau$. This population reduces by those who recover due to the effective treatment at the rate r_1, TB-induce death at the rate d_2 and natural death at the rate μ. Thus,

$$\frac{dJ}{dt} = \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J.$$

The population of recovered individuals increases by those that recovered from the disease at the rate r_1 and reduces by natural death at the rate μ. Hence the equation:

$$\frac{dR}{dt} = r_1 J - \mu R$$

General transfer diagram for the model

From the assumptions presented (above) and the model description provided (above) the model flow diagram is presented (Figure 1).

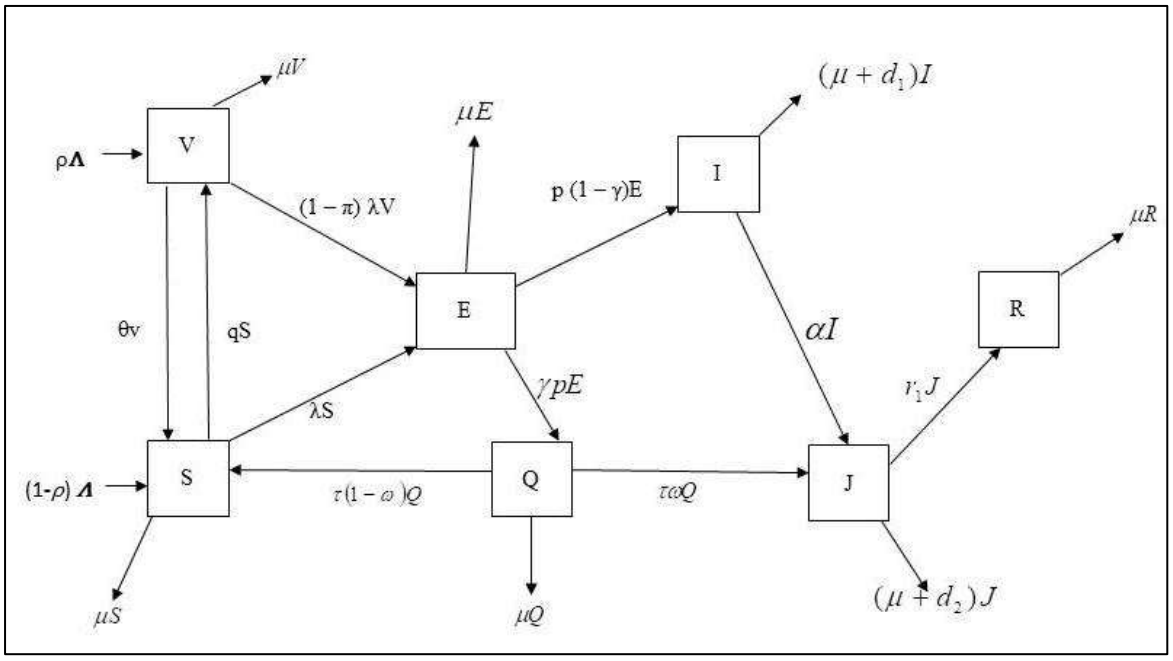

Figure 1: A general transfer diagram for the modified model (SEIQJVR)

The Model equations (model with constant controls)

Based on the assumptions, the description and the schematic flow diagram of the model in Figure 1, we present the following set of first order nonlinear ordinary differential equation for the modified model (SVEQIJR).

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\rho)\Lambda + \theta V + (1-\omega)\tau Q - (\lambda + q + \mu)S,\\
\frac{dV}{dt} &= \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V,\\
\frac{dE}{dt} &= (S + (1-\pi)V)\lambda - (p + \mu)E,\\
\frac{dQ}{dt} &= p\gamma E - (\tau + \mu)Q,\\
\frac{dI}{dt} &= p(1-\gamma)E - (\alpha + d_1 + \mu)I,\\
\frac{dJ}{dt} &= \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J,\\
\frac{dR}{dt} &= r_1 J - \mu R,\\
&\text{where}\\
\lambda &= \frac{\beta(I + \eta J)}{N},\\
N(t) &= S(t) + V(t) + E(t) + Q(t) + I(t) + J(t) + R(t).
\end{aligned}
\tag{3.2}
$$

Subject to the following initial condition:

$$S(0) > 0, V(0) \geq 0, E(0) \geq 0, Q(0) \geq 0, I(0) \geq 0, J(0) \geq 0, R(0) \geq 0.$$

Methods of Analysis

The following methods will be employed for the analysis of the modified model:

(i) Cauchy-Lipchitz condition will be used to check for the existence and uniqueness of model solution;

(ii) Separation of variables and method of integrating factor in conjunction with comparison theorem will be used for positivity and boundedness of the model solution;

(iii) The method of the next generation matrix will be used to compute the basic reproduction number and the local stability analysis of disease free equilibrium point of the model;

(iv) The approach by Castillo-Chavez, (2000) will be used for the global stability analysis of the disease free equilibrium point of the model;

(v) The method of Lyapunov function in conjunction with Lassalle invariance principle will be used to establish the global stability analysis of the endemic equilibrium point of the model;

(vi) Normalized forward sensitivity index will be used for the sensitivity of the model parameters with respect to the basic reproduction number;

Theorem 2.1 (Jishan & Wei-Ping, 2004).
Consider the following initial valued problem (IVP)

$$y' = f(t, y_1, y_2, \dots y_n), y(t_0) = y_0, y_1(t_0) = y \dots y_n(t_0) = y_n \quad (2.2)$$

Let D, denote the region.

$$|t - t_0| \le a, \|y - y_0\| \le b, y = (y_1, y_2, \dots y_n),$$
$$y_0 = (y_{10}, y_{20}, y_{30}, \dots y_{n0}). \quad (2.3)$$

Suppose that $f(t, y)$ satisfied the Lipchitz condition

$$\|f(t, y_n) - f(t, y_{n-1})\| \le k\|y_n - y_{n-1}\|, n = 1,2,3 \dots \quad (2.4)$$

Whenever the pair (t, y_n) and (t, y_{n-1}) belong to D where k is a positive constant called Lipchitz constant, then there exist a constant $\delta > 0$ such that a unique continuous vector solution given by y(t) of the system (2.2) in the interval $|t - t_o| < \delta$, exists.

It is important to note that condition (2.3) is satisfied by the requirement that $\frac{\partial f_i}{\partial y_j}, (\forall i, j = 1, 2, 3, \dots, n)$ be continuous and bounded in the region D.

Lemma 2.1: (Jishan & Wei-Ping, 2004).

If $f(t, y)$ has continuous partial derivative $\frac{\partial f_i}{\partial y_i}$ for $i = 1, 2, \cdots, n$ on a bounded convex domain D then it satisfies a Lipchitz condition in D

Boundedness and positivity of the solutions

The method of integration in conjunction with comparison theorem to check for the positivity and boundedness of the model solution will be used.

Equilibrium points of the model

The disease-free equilibrium point of the model equation given by system (2.1) will be obtained by setting the right-hand side of equation (2.1) to zero and then solve for the associated state variables in the absence of infection.

The basic reproduction number

According to Driessche and Watmough (2002), the basic reproduction number is defined as the expected number of secondary cases of infections arising from a single infected case in a completely susceptible population during the entire period of infectiousness. Basic reproduction number is a key concept in epidemiology. It serves as a threshold parameter that predicts whether an infection dies out or persists. If $R_0 < 1$, then, on average, infectious individuals introduced in a population produce less than one new infection during their period of infectiousness. On the other hand, if $R_0 > 1$ then each infected individual produces, on average, more than one new infection, and the disease will persist in the population. Assume that there are n compartments so that the first m compartments correspond to infected individuals.

Let $F_i(x)$ be the rate of appearance of new infections in compartments i, while $V^*_i(x)$ be the rate of transfer of individuals into compartment *i*. The disease transmission model consists of the system of equations $y_i^{'} = F_i(x) - V_i(x)$.

The basic reproductive number (reproduction ratio) R_0 is then defined as $R_0 = \rho\left[FV^{-1}\right]$, where ρ is the spectral radius of the next generation matrix (Diekmann et al,. (1990).

Local stability of the disease-free equilibrium point of the model DFE

The local stability analysis of the DFE of the modified model will be analyzed using linearization method.

Definition 2.1

The Jacobian matrix of f in equation (2.1) evaluated at the equilibrium point x_e, denoted by $Df(x_e)$ is the matrix, $Df(x_e)$ of partial derivatives of f evaluated at x_e i.e.

$$Df(x_e) = \begin{bmatrix} \frac{\partial f_1(x_e)}{\partial x_1} & \cdots & \frac{\partial f_1(x_e)}{\partial x_n} \\ \vdots & \vdots & \vdots \\ \frac{\partial f_n(x_e)}{\partial x_1} & \cdots & \frac{\partial f_n(x_e)}{\partial x_n} \end{bmatrix}$$

Theorem 2.2

Suppose all the eigen values of $Df(x_e)$ have negative real parts. Then the equilibrium point $x = x_e$ of the system (2.2) is locally asymptotically stable, and unstable if at least one of the eigen values has positive real part.

Theorem 2.3 (Wiggins, 1983)

Consider the following autonomous system

$$\frac{dx(t)}{dt} = f(x(t)), t \geq 0 \qquad (2.5)$$

$$x(0) = x_0 \in R^n$$

Let, x_e be an equilibrium point of system (2.2) and let $V : U \to R$ be a C^1 function defined on some neighborhood U of x_e such that

i. V positive – definite,

ii. $\frac{dV}{dt} \leq 0$ in $U - \{x_e\}$,

iii. $\frac{dV}{dt} < 0$ in $U - \{x_e\}$,

then x_e is asymptotically stable.

Note that any function V that satisfies the conditions (i) and (ii) above is called a Lyapunov function.

Definition 2.2 Invariant Set (Barbashin, 1970)

A set M is said to be invariant with respect to system (2.2) if $x_0 \in M$, implies $x(t, x_0) \in M$ for all $t \in R$. A set M is positively invariant with respect to system (2.2) if for $x \in M, x(t, x_0) \in M$ for all $t > 0$. Similarly, a set M is negatively invariant with respect to system (3.4) if for all $x \in M, x(t, x_0) \in M$ for all $t < 0$.

Theorem 2.4 (LaSalle Invariant Principle (LaSalle, 1976)

Suppose that the equilibrium point of system (2.2) $x_e = 0$ and V is a Lyapunov function on some neighborhood U of $x_0 = 0$. If $x_0 \in U$ has its forward trajectory bounded with limit points in U and M is the largest invariant set of $E = \left\{ x_e \in U : \dot{V} = 0 \right\}$, then $\phi(x_0, t) \to M$ as $t \to \infty$.

Results

Existence and Uniqueness of the Model Solution

For the purpose of showing the existence and uniqueness of model solution the following representations were made:

Let $y_1(t) = S(t), y_2(t) = V(t), y_3(t) = E(t), y_4(t) = Q(t), y_5(t) = I(t), y_6(t) = J(t), y_7(t) = R(t)$, so that the model equation given by system (3.2) can be rewritten in a compact form as;

$$\frac{dy}{dt} = f\left(t, y_1, y_2, y_3, ..., y_7\right), y_1\left(t_0\right) = y_{10}, y_2\left(t_0\right) = y_{20}, y_3\left(t_0\right) = y_{30}, ..., y_7\left(t_0\right) = y_{70} \qquad (2.6)$$

Theorem 2.5:

Suppose that the function $f\left(t, y_1, y_2, y_3, ..., y_7\right)$ in the model equation given by system (4.1) satisfies Lipchitz condition in the region $D = \left\{(t, y) : 0 \le |t - t_0| \le a, 0 \le \|y - y_0\| \le b\right\}$ for some $a > 0, b > 0,$ a, b ∈, then there exists a constant number $\delta_1 > 0$, such that a unique continuous vector solution $y(t)$ of the model equation given by system (2.6) exists in the interval $|t - t_0| < \delta_1$.

Proof:

From the model equation given by system (2.1) let

$$\left.\begin{aligned}
f_1(t, y_1) &= \frac{dS}{dt} = (1-\rho)\Lambda + \theta V + (1-\omega)\tau Q - (\lambda + q + \mu)S, \\
f_2(t, y_2) &= \frac{dV}{dt} = \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V, \\
f_3(t, y_3) &= \frac{dE}{dt} = (S + (1-\pi)V)\lambda - (p + \mu)E, \\
f_4(t, y_4) &= \frac{dQ}{dt} = p\gamma E - (\tau + \mu)Q, \\
f_5(t, y_5) &= \frac{dI}{dt} = p(1-\gamma)E - (\alpha + d_1 + \mu)I, \\
f_6(t, y_6) &= \frac{dJ}{dt} = \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J, \\
f_7(t, y_7) &= \frac{dR}{dt} = r_1 J - \mu R,
\end{aligned}\right\} \qquad (4.2)$$

According Lemma (2.1), for the functions given by equation (2.7) to satisfy Lipchitz condition. It is sufficient to show that $\frac{\partial f_i}{\partial y_j}, (i, j = 1, 2, 3, \cdots, 7)$ are continuous and bounded in the region D.

The partial derivatives of the functions (2.7) are:

$$\left|\frac{\partial f_1}{\partial S}\right| = \left|-(q+\mu+\lambda)\right| = (q+\mu+\lambda) < \infty, \left|\frac{\partial f_1}{\partial V}\right| = \theta < \infty, \left|\frac{\partial f_1}{\partial E}\right| = 0 < \infty, \left|\frac{\partial f_1}{\partial Q}\right| = (1-\omega)\tau < \infty, \left|\frac{\partial f_1}{\partial I}\right| = 0 < \infty, \left|\frac{\partial f_1}{\partial J}\right| = 0 < \infty, \left|\frac{\partial f_1}{\partial R}\right| = 0 < \infty \quad (2.8)$$

Also, taking the partial derivatives of the second component of equation (2.7) we obtained

$$\left|\frac{\partial f_2}{\partial S}\right| = q < \infty, \left|\frac{\partial f_2}{\partial V}\right| = \left|-\left(\theta + (\mu+\pi)\lambda + \mu\right)\right| = \left(\theta + (\mu+\pi)\lambda + \mu\right) < \infty = \left|\frac{\partial f_2}{\partial E}\right| = 0 < \infty, \left|\frac{\partial f_2}{\partial Q}\right| = 0 < \infty, \left|\frac{\partial f_2}{\partial I}\right| = 0 < \infty, \quad (4.4)$$

$$\left|\frac{\partial f_2}{\partial J}\right| = 0 < \infty. \quad (4.4)$$

Considering the partial derivatives of the third component of equation (4.2) we get

$$\left|\frac{\partial f_3}{\partial S}\right| = |\lambda| < \infty, \left|\frac{\partial f_3}{\partial V}\right| = (1-\pi)\lambda < \infty, \left|\frac{\partial f_3}{\partial E}\right| = \left|-(p+\mu)\right| = (p+\mu) < \infty, \left|\frac{\partial f_3}{\partial Q}\right| = 0 < \infty, \left|\frac{\partial f_3}{\partial I}\right| = 0 < \infty, \left|\frac{\partial f_3}{\partial J}\right| = 0 < \infty, \left|\frac{\partial f_3}{\partial R}\right| = 0 < \infty$$

(2.7)

The partial derivatives of the fourth component of equation (4.2) are as follows:

$$\left|\frac{\partial f_4}{\partial S}\right| = 0 < \infty, \left|\frac{\partial f_4}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_4}{\partial E}\right| = p\gamma < \infty, \left|\frac{\partial f_4}{\partial Q}\right| = \left|-(\tau+\mu)\right| = (\tau+\mu) < \infty, \left|\frac{\partial f_4}{\partial I}\right| = 0 < \infty, \left|\frac{\partial f_4}{\partial J}\right| = 0 < \infty, \left|\frac{\partial f_4}{\partial R}\right| = 0 < \infty \quad (4.6)$$

The partial derivatives of the fifth component of equation (2.7) are:

$$\left|\frac{\partial f_5}{\partial S}\right| = 0 < \infty, \left|\frac{\partial f_5}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_5}{\partial E}\right| = \left|p(1-\gamma)\right| < \infty, \left|\frac{\partial f_5}{\partial Q}\right| = 0 < \infty, \left|\frac{\partial f_5}{\partial I}\right| = \left|-(\alpha+\mu+d_1)\right| = (\alpha+\mu+d_1) < \infty, \left|\frac{\partial f_5}{\partial J}\right| = 0 < \infty, \left|\frac{\partial f_5}{\partial R}\right| = 0 < \infty$$

(2.12)

The partial derivatives of the sixth component of equation (2.7) are:

$$\left|\frac{\partial f_6}{\partial S}\right| = 0 < \infty, \left|\frac{\partial f_6}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_6}{\partial E}\right| = 0 < \infty, \left|\frac{\partial f_6}{\partial Q}\right| = \tau\omega < \infty, \left|\frac{\partial f_6}{\partial I}\right| = \alpha < \infty, \frac{\partial f_6}{\partial J} = \left|-(r_1+\mu+d_2)\right| = (r_1+\mu+d_2) < \infty, \left|\frac{\partial f_6}{\partial R}\right| = 0 < \infty$$

(2.13)

The partial derivatives of the seventh component of equation (2.7) are:

$$\left|\frac{\partial f_7}{\partial S}\right| = 0 < \infty, \left|\frac{\partial f_7}{\partial V}\right| = 0 < \infty, \left|\frac{\partial f_7}{\partial E}\right| = 0 < \infty, \left|\frac{\partial f_7}{\partial Q}\right| = 0 < \infty, \left|\frac{\partial f_7}{\partial I}\right| = 0 < \infty, \left|\frac{\partial f_7}{\partial J}\right| = r_1 < \infty, \left|\frac{\partial f_7}{\partial R}\right| = |-\mu| = \mu < \infty$$

(2.14)

It can be observed from equations (2.7) – (2.1.4) that all the partial derivatives of the functions are continuous and bounded in the interval $0 < D < \infty$. Thus, by the Lemma 2.1. the functions given by equation (2.7) satisfy Lipchitz condition and hence, there exists a unique solution of model equation in the region D.

Positivity of the Model Solution

Since the model monitors human population, it is important to establish that for a given nonnegative initial conditions, the model solution will remain positive for all time. This will be achieved using the following theorem:

Theorem 2.6:

For non-negative initial conditions for the model equation given by system (2.1) the solutions (S, V, E, Q, I, J, R) of the model equation are all non-negative for all time $t \geq 0$.

Proof:

For the model equations in the system (2.1), let t^* be the maximum time for the epidemics. This implies that;

$t^* = Sup\{t^* > 0 : (S > 0, V > 0, E > 0, Q > 0, I > 0, J > 0, R > 0)\}$, thus, $t^* \geq 0$. From the first equation of system (2.1), we have

$$\frac{dS}{dt} = (1-\rho)\Lambda + \theta V + (1-\omega)Q - (\lambda + q + \mu)S \geq -(\lambda + q + \mu)S \tag{2.15}$$

Integrating equation (2.1.5), from $t = 0$ to t=t^* we have

$$\int_0^{t^*} \frac{dS}{S} \geq -\left((q+\mu)\int_0^{t^*} dt + \int_0^{t^*} \lambda(u)\,du \right),$$

$$\ln(S) \geq -\left((q+\mu)t^* + \int_0^{t^*} \lambda(u)\,du \right), \tag{2.16}$$

Taking exponential of both sides of equation (2.1.6) and evaluate the limits to obtain

$S(t^*) \geq S(0)e^{-\left((q+\mu)t^* + \int_0^{t^*}\lambda(u)du\right)} \geq 0$, hence, $S(t^*) \geq 0$. This implies that $S(t) \geq 0$ for all $t > 0$. Similarly taking the second component of system (2.1) will be:

$$\frac{dV}{dt} = \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V$$

$$\frac{dV}{dt} \geq -((1-\pi)\lambda + \theta + \mu)V \tag{2.17}$$

Integrating equation (2.1.7), from $t = 0$ to t=t^* to have:

$$\int_0^{t^*} \frac{dV}{V} \geq -\left((\theta+\mu)\int_0^{t^*} dt + (1-\pi)\int_0^{t^*} \lambda(u)\,du \right), \tag{2.18}$$

$$\ln(V) \geq -\left((\theta+\mu)t^* + (1-\pi)\int_0^{t^*} \lambda(u)\,du \right),$$

Taking exponential of both sides of equation (2.18) and evaluate the limits we obtain

$V(t^*) \geq V(0)e^{-\left((\theta+\mu)t^* + (1-\pi)\int_0^{t^*}\lambda(u)du\right)} \geq 0$. Hence, $V(t) \geq 0$ for all $t > 0$.

From the third equation of system (2.1), we have

$$\frac{dE}{dt} = (S + (1-\pi)V)\lambda - (p+\mu)E, \tag{2.19}$$

$$\frac{dE}{dt} \geq -(p+\mu)E,$$

Integrating equation (2.19) from $t = 0$ to t=t^* and evaluate the limits we get

$E(t^*) \geq E(0)e^{-(p+\mu)t^*} \geq 0$, hence from $E(t) \geq 0$ for all $t > 0$. Also, from the fourth equation of system (2.1), we have

$$\frac{dQ}{dt} = p\gamma E + \phi_1 - (\tau+\mu)Q, \tag{2.20}$$

$$\frac{dQ}{dt} \geq -(\tau+\mu)Q$$

Integrating equation (2.20) from $t = 0$ to t=t^* and evaluate the limits we obtain

$Q(t^*) \geq Q(0)e^{-(\tau+\mu)t^*} \geq 0$. Therefore, $Q(t) \geq 0$ for all $t > 0$.

From the fifth equation of system (3.2), we have

$$\frac{dI}{dt} = p(1-\gamma)E + \phi_2 - (\alpha + d_1 + \mu)I,$$
$$\frac{dI}{dt} \geq -(\alpha + d_1 + \mu)I \quad (2.21)$$

Integrating equation (2.21) from $t = 0$ to t=t^* and evaluate the limits we obtain

$I(t^*) \geq I(0)e^{-(\alpha+\mu+d_1)t^*} \geq 0$. Thus, $I(t) \geq 0$. From the sixth equation of system (2.1), we have

$$\frac{dJ}{dt} = \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J,$$
$$\frac{dJ}{dt} \geq -(r_1 + d_2 + \mu)J \quad (2.22)$$

Integrating equation (2.22) from $t = 0$ to t=t^* and evaluate the limits we obtain

$J(t^*) \geq J(0)e^{-(r_1+d_2+\mu)t^*} \geq 0$. Hence $J(t) \geq 0$ for all $t > 0$. Similarly, from the last equation of system (3.2), we have

$$\frac{dR}{dt} = r_1 J - \mu R,$$
$$\frac{dR}{dt} \geq -\mu R \quad (2.23)$$

Integrating equation (2.23) from $t = 0$ to t=t^* and evaluate the limits we obtain

$R(t^*) \geq R(0)e^{-\mu t^*} \geq 0$. Thus, $R(t) \geq 0$ for all $t > 0$. Hence we have shown that model solution with non-negative initial condition will remain non-negative for all $t > 0$.

Feasible region (Invariant region)

The region in which the solution of the model equations given by system (2.1) will be bounded and make biological sense can be established in the following theorem:

Theorem 2.7:

The solution of the model given by system (2.1) is bounded in the
The closed set

$\Omega = \{S, V, E, Q, I, J, R) \in R_+^7 : N(t) \leq \frac{\Lambda}{\mu}\}$.

Furthermore, the set Ω is positively invariant and attracting with respect to model equation given by system (2.1).

Proof:

Given that

$$N(t) = S(t) + V(t) + E(t) + Q(t) + I(t) + J(t) + R(t) \quad (2.24)$$

Differentiating equation (2.24) with respect to time t we have

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dE}{dt} + \frac{dQ}{dt} + \frac{dI}{dt} + \frac{dJ}{dt} + \frac{dR}{dt} \quad (2.25)$$

Substituting the right hand sides of equation (2.1) into equation (2.25) we have

$$\frac{dN}{dt} = \Lambda - \mu(S + V + E + Q + I + J + R) - d_1 I - d_2 J$$

$$\frac{dN}{dt} = \Lambda - \mu N - d_1 I - d_2 J \quad (2.26)$$

In the absence of TB-induced death rate i.e. $d_1 = d_2 = 0$, equation (2.26) becomes

$$\frac{dN}{dt} \le \Lambda - \mu N$$

This equation can also be rewritten as

$$\frac{dN}{dt} + \mu N \le \Lambda \qquad (2.27)$$

By applying the method of integrating factor to solve equation (2.27).

$$N(t) \le N(0)e^{-\mu t} + \frac{\Lambda}{\mu}\left(1 - e^{-\mu t}\right) \qquad (2.28)$$

$$\limsup_{t\to\infty} N(t) \le \frac{\Lambda}{\mu}. \qquad (2.29)$$

Therefore, the model solution is bounded by $0 \le N(t) \le \frac{\Lambda}{\mu}$. In particular from equation (2.29), if $N(0) \le \frac{\Lambda}{\mu}$, then $N(t) \le \frac{\Lambda}{\mu}$. Therefore, the set Ω is positively invariant, meaning that all the solution that starts in Ω remain in Ω for all t > 0. In addition, if $N(0) \ge \frac{\Lambda}{\mu}$, then either the solution enters the region Ω in finite time or $N(t)$ approaches $\frac{\Lambda}{\mu}$ asymptotically. Hence, we conclude that Ω is an attracting set in R_+^7.Therefore the model equation given by system (2.1) is mathematically and epidemiologically well posed in this region.

The Disease-Free Equilibrium (DFE) Point of the Model

The disease-free equilibrium (DFE) points are steady state solutions that depict the absence of the disease in the population. This implies that at the TB-free equilibrium (DFE) point by setting the right hand sides of equation (2.1) to zero i.e. $\frac{dS}{dt} = \frac{dV}{dt} = \frac{dE}{dt} = \frac{dQ}{dt} = \frac{dI}{dt} = \frac{dJ}{dt} = \frac{dR}{dt} = 0$ and then set all parameters and state variables related to TB to zero i.e. $E = I = Q = J = 0 = R = 0$.

Therefore we have

$$\begin{aligned} &(1-\rho)\Lambda + \theta V - (q+\mu)S = 0 \\ &\rho\Lambda + qS - (\theta+\mu)V = 0 \end{aligned} \qquad (2.30)$$

By writing equation (2.30) in vector, form it will be

$$\begin{bmatrix} (q+\mu) & -\theta \\ -q & (\theta+\mu) \end{bmatrix} \begin{bmatrix} S \\ V \end{bmatrix} = \begin{bmatrix} (1-\rho)\Lambda \\ \rho\Lambda \end{bmatrix}$$

Applying the crammer's rule.

let D, D_1, D_2 be defined by

$$|D| = \begin{vmatrix} (q+\mu) & -\theta \\ -q & (\theta+\mu) \end{vmatrix} = q\mu + \mu(\theta+\mu)$$

$$|D| = \mu(q+\theta+\mu) \qquad (2.31)$$

$$|D_1| = \begin{vmatrix} (1-\rho)\Lambda & -\theta \\ \rho\Lambda & (\theta+\mu) \end{vmatrix} = (1-\rho)(\theta+\mu)\Lambda + \theta\rho\Lambda \qquad (2.32)$$

$$|D_2| = \begin{vmatrix} (q+\mu) & (1-\rho)\Lambda \\ -q & \rho\Lambda \end{vmatrix} = (q+\mu)\rho\Lambda + (1-\rho)q\Lambda \qquad (2.33)$$

Using the formula $S^0=\frac{|D_1|}{|D|}$ and $V^0=\frac{|D_2|}{|D|}$ we have

$S^0=\frac{\Lambda\left((1-\rho)\mu+\theta\right)}{\mu\left(\mu+q+\theta\right)}$, $V^0=\frac{\Lambda\left(\mu\rho+q\right)}{\mu\left(\mu+q+\theta\right)}$. Thus, the DFE is given by

$$X_0=\left(S^0,V^0,E^0,Q^0,I^0,J^0,R^0\right)=\left(\frac{\Lambda\left((1-\rho)\mu+\theta\right)}{\mu\left(\mu+q+\theta\right)},\frac{\Lambda\left(\mu\rho+q\right)}{\mu\left(\mu+q+\theta\right)},0,0,0,0,0\right) \quad (2.34)$$

The Endemic-Equilibrium (EFE) Point of the Model

The endemic equilibrium point of model describe the persistence of TB in the population i.e. $S>0,V>0,E>0,Q>0,I>0,J>0,R>0$. To obtain the endemic equilibrium point of the model the right hand side of the model equation (2.1) is set to zero and then solve for the associated state variables at the steady state $S^*,V^*,E^*,Q^*,I^*,J^*,R^*$. Thus, at the equilibrium point, the model equation (2.1) becomes

$$\begin{aligned}
&(1-\rho)\Lambda+\theta V^*+(1-\omega)\tau Q^*-\left(\lambda^*+q+\mu\right)S^*=0,\\
&\rho\Lambda+qS^*-\left(\theta+(1-\pi)\lambda^*+\mu\right)V^*=0,\\
&\left(S^*+(1-\pi)V^*\right)\lambda^*-(p+\mu)E^*=0^*,\\
&p\gamma E^*-(\tau+\mu)Q^*=0,\\
&p(1-\gamma)E^*-(\alpha+d_1+\mu)I^*=0,\\
&\alpha I^*+\tau\omega Q^*-(r_1+d_2+\mu)J^*=0,\\
&r_1J^*-\mu R^*=0,
\end{aligned} \quad (2.35)$$

Solving for the state variables at the steady state give us endemic equilibrium point of the system.

From the first equation of system (2.35);

$$S^*=\frac{(1-\rho)\Lambda+\theta V^*+(1-\omega)\tau Q^*}{\left(\lambda^*+q+\mu\right)} \quad (2.36)$$

From the second equation of system (2.35)

$$V^*=\frac{\rho\Lambda}{\left(\theta+(1-\pi)\lambda^*+\mu\right)}+\frac{qS^*}{\left(\theta+(1-\pi)\lambda^*+\mu\right)} \quad (2.37)$$

From the third equation of system (2.35);

$$E^*=\frac{\left(S^*+(1-\pi)V^*\right)\lambda^*}{(p+\mu)} \quad (2.38)$$

Using the fourth equation of system (2.35):

$$Q^{\bullet}=\frac{p\gamma E^*}{1+\mu} \quad (2.39)$$

From the fifth equation of system (2.35):

$$I^{\bullet}=\frac{p(1-\gamma)E^*}{(\alpha+\mu+d_1)} \quad (2.40)$$

From the sixth equation of system (2.35):

$$J^*=\frac{\alpha I^*+\tau\omega Q^*}{r_1+d_2+\mu} \quad (2.41)$$

From the seventh equation of system (2.35):

$$R^* = \frac{r_1 J^*}{\mu} \tag{2.42}$$

Thus, the endemic equilibrium point of the model is given by

$$X_1 = \left(S^*, V^*, E^*, Q^*, I^*, J^*, R^*\right), \tag{2.43}$$

where $S^*, V^*, E^*, Q^*, I^*, J^*$ and R^* are defined in equations (2.36)-(2.43) respectively.

The Basic Reproduction Number

The basic reproduction number is defined as the average number of secondary cases of infections generated by a typical infected person in an otherwise disease free population. The basic reproduction number (R_0) of the system (2.1) is computed using the next generation matrix method. Here the matrix F_i denotes the rates of appearance of new infections and V_i represents the transfer of infection into and out of any compartment respectively. The matrices are given by

$$F_i = \begin{bmatrix} \frac{(1-\pi)\beta(I+\eta J)V}{N} + \frac{\beta(I+\eta J)S}{N} \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad V_i = \begin{bmatrix} (p+\mu)E \\ -p\gamma E + (\tau+\mu)Q \\ -p(1-\gamma)E + (\alpha + d_1 + \mu)I \\ -\alpha I - \tau\omega Q + (r_1 + d_2 + \mu)J \end{bmatrix} \tag{2.44}$$

Then F_i and V_i are evaluated by taking the partial derivatives of the terms in F_i and V_i at the disease-free equilibrium to obtain a non-negative square matrix F and a non-singular matrix V.

$$F = \frac{\partial F_i(X_0)}{\partial x_j}$$

$$= \begin{bmatrix} \frac{\partial f_1(X_0)}{\partial E} & \frac{\partial f_1(X_0)}{\partial Q} & \frac{\partial f_1(X_0)}{\partial I} & \frac{\partial f_1(X_0)}{\partial J} \\ \frac{\partial f_2(X_0)}{\partial E} & \frac{\partial f_2(X_0)}{\partial Q} & \frac{\partial f_2(X_0)}{\partial I} & \frac{\partial f_2(X_0)}{\partial J} \\ \frac{\partial f_3(X_0)}{\partial E} & \frac{\partial f_3(X_0)}{\partial Q} & \frac{\partial f_3(X_0)}{\partial I} & \frac{\partial f_3(X_0)}{\partial J} \\ \frac{\partial f_4(X_0)}{\partial E} & \frac{\partial f_4(X_0)}{\partial Q} & \frac{\partial f_4(X_0)}{\partial I} & \frac{\partial f_4(X_0)}{\partial J} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{(1-\pi)\beta V^0}{N} + \frac{\beta S^0}{N} & \frac{(1-\pi)\beta\eta V^0}{N} + \frac{\beta\eta S^0}{N} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{(1-\pi)\beta(\mu\rho+q)}{q+\theta+\mu} + \frac{\beta(1-\rho)\mu+\theta}{q+\theta+\mu} & \frac{(1-\pi)\beta\eta(\mu\rho+q)}{q+\theta+\mu} + \frac{\beta\eta(1-\rho)\mu+\theta}{q+\theta+\mu} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{2.45}$$

$$V = \frac{\partial V_i(X_0)}{\partial x_j}$$

$$= \begin{bmatrix} \frac{\partial V_1(X_0)}{\partial E} & \frac{\partial V_1(X_0)}{\partial Q} & \frac{\partial V_1(X_0)}{\partial I} & \frac{\partial V_1(X_0)}{\partial J} \\ \frac{\partial V_2(X_0)}{\partial E} & \frac{\partial V_2(X_0)}{\partial Q} & \frac{\partial V_2(X_0)}{\partial I} & \frac{\partial V_2(X_0)}{\partial J} \\ \frac{\partial V_3(X_0)}{\partial E} & \frac{\partial V_3(X_0)}{\partial Q} & \frac{\partial V_3(X_0)}{\partial I} & \frac{\partial V_3(X_0)}{\partial J} \\ \frac{\partial V_4(X_0)}{\partial E} & \frac{\partial V_4(X_0)}{\partial Q} & \frac{\partial V_4(X_0)}{\partial I} & \frac{\partial V_4(X_0)}{\partial J} \end{bmatrix}$$

$$= \begin{bmatrix} (p+\mu) & 0 & 0 & 0 \\ -p\gamma & \tau+\mu & 0 & 0 \\ -p(1-\gamma) & 0 & (\alpha+d_1+\mu) & 0 \\ 0 & -\omega\tau & \alpha & (r_1+d_2+\mu) \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{1}{p+\mu} & 0 & 0 & 0 \\ \frac{p\gamma}{(p+\mu)(\tau+\mu)} & \frac{1}{(\tau+\mu)} & 0 & 0 \\ \frac{p(1-\gamma)}{(p+\mu)(\alpha+d_1+\mu)} & 0 & \frac{1}{(\alpha+d_1+\mu)} & 0 \\ \frac{p[\alpha(\tau+\mu)(1-\gamma)+(\alpha+d_1+\mu)\omega\tau\gamma]}{(p+\mu)(\tau+\mu)(\alpha+d_1+\mu)(r_1+\mu+d_2)} & \frac{\omega\tau}{(\tau+\mu)(r_1+\mu+d_2)} & \frac{\alpha}{(\alpha+d_1+\mu)(r_1+\mu+d_2)} & \frac{1}{(r_1+\mu+d_2)} \end{bmatrix}$$

$$= \begin{bmatrix} \frac{1}{k_1} & 0 & 0 & 0 \\ \frac{p\gamma}{k_1k_2} & \frac{1}{k_2} & 0 & 0 \\ \frac{pM}{k_1k_3} & 0 & \frac{1}{k_3} & 0 \\ \frac{p(-\gamma\omega\tau k_3+M\alpha k_2}{k_1k_2k_3k_4} & \frac{\omega\tau}{k_2k_4} & -\frac{\alpha}{k_3k_4} & \frac{1}{k_4} \end{bmatrix}, \quad (2.46)$$

(2.47)

Where

$k_1 = p+\mu, k_2 = \tau+\mu, k_3 = \alpha+d_1+\mu, k_4 = r_1+d_2+\mu$

$$FV^{-1} = \begin{bmatrix} A_{11} & A_{12} & A_{13} & A_{14} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad (2.48)$$

with $A_{11}=\frac{(M(\alpha\eta+k_4)k_2+\gamma\omega k_3\eta\tau)p\beta((C\rho+L)\mu+Cq+\theta)}{(\mu+q+\theta)k_1k_2k_3k_4}$, $A_{12}=\frac{\omega\tau\beta\eta((C\rho+L)\mu+Cq+\theta)}{(\mu+q+\theta)k_2k_4}$,

$A_{13}=\frac{(-\alpha\eta+k_4)((C\rho+L)\mu+Cq+\theta)\beta}{(\mu+q+\theta)k_3k_4}$, $A_{14}=\frac{\beta((C\rho+L)\mu+Cq+\theta)\eta}{(\mu+q+\theta)k_4}$ and $M = 1-\gamma,\ L = 1-\rho, C = 1-\pi$

$$\left|FV^{-1}-\lambda I\right| = \begin{vmatrix} A_{11}-\lambda_1 & A_{12} & A_{13} & A_{14} \\ 0 & -\lambda_2 & 0 & 0 \\ 0 & 0 & -\lambda_3 & 0 \\ 0 & 0 & 0 & -\lambda_4 \end{vmatrix} = 0 \quad (2.49)$$

The simplified characteristics polynomial is given by

$$(A_{11}-\lambda_1)(-\lambda_2)(-\lambda_3)(-\lambda_4) = 0 \quad (2.50)$$

The eigenvalues of the characteristics polynomial in equation (4.40) are as follows:

$$\lambda_1 = A_{11}, \lambda_2 = \lambda_3 = \lambda_4 = 0 \quad (2.51)$$

Therefore, from equation (4.41), the dominant eigenvalue is λ_1 therefore the basic reproduction number R_0 is given by

$$R_0=\frac{(1-\gamma)(\alpha\eta+r_1+d_2+\mu)(\tau+\mu)+\gamma\omega(\alpha+d_1+\mu)\eta\tau)p\beta(1-\pi)p+(1-\rho)\mu+(1-\pi)q+\theta)}{(\mu+q+\theta)(\tau+\mu)(p+\mu)(\alpha+d_1+\mu)(r_1+d_2+\mu)} \quad (2.52)$$

The Local Stability Analysis of the DFE of the Model

Having computed the basic reproduction number of the disease the following theorem follows directly from Theorem 2 of Van den et al,. (2002).

Theorem 2.8

The disease-free equilibrium point of the model equation given by system (2.1) is locally asymptotically stable whenever $R_0 < 1$ and unstable otherwise.

Remark

Epidemiologically, the results in Theorem 2.8 implies that when $R_0 < 1$, on the average each infected individual infects less than one individual and the TB will die out. On the other hand, if $R_0 > 1$ then on the average each infected individual infects more than one other individual and we would expect the TB to spread in the population.

The Global Stability Analysis of the Disease Free Equilibrium Point of the Model

The result in Theorem 2.8 implies that the TB can be eliminated from the population (when $R_0 < 1$) if the initial size of the sub-populations of the model given by system (2.1) are in the basin of attraction of the DFE (X_0) .To ensure that the elimination of TB is independent of the initial sizes of the sub-populations of the model (when $R_0 < 1$), it is necessary to show that the DFE is globally-asymptotically stable (GAS). This will be established using the method by Castillo-Chavez, (2000). The model equation given by system (2.1) is rewritten as:

$$\begin{aligned} \frac{dX}{dt} &= F(X, Z), \\ \frac{dZ}{dt} &= G(X, Z), G(X, 0) = 0 \end{aligned} \quad (2.53)$$

Where $X = (S, V, R,) \in R_+^3$ represents the subpopulation of uninfected individuals and $Z = (E, Q, I, J) \in R_+^4$represents the subpopulation of infected individuals. Suppose $E_0 = (X_0, 0)$ represents the disease-free equilibrium point of the system (2.53) E_0 of the model to be globally asymptotically stable the following conditions H1 and H2 must be satisfied:

$H1: \frac{dX}{dt} = F(X,0)$, E_0 is globally asymptotically stable.

$H2: \frac{dZ}{dt} = AZ - G(X,Z), G(X,Z) \geq 0$ for all $(X,Z) \in \Omega$, where A=$D_z G(X,0) Z$ is an M-matrix (the off diagonal elements of A are nonnegative).

Theorem 2.9:

The equilibrium point of the model given by $E_0 = (X_0, 0)$ is globally asymptotically stable if $R_0 < 1$ and conditions H1 and H2 are satisfied.

Proof:

The proof begins by defining new variables and breaking the model equations given by system (2.1) into the subsystems given in equation (2.53) as follows:

$$\begin{aligned} \frac{dX}{dt} &= F(X,Z), \\ \frac{dZ}{dt} &= G(X,Z), G(X,0) = 0 \end{aligned} \qquad (2.54)$$

The disease free equilibrium is now denoted by $E_0 = (X_0, 0)$, where $X_0 = \left(\frac{\Lambda((1-\rho)\mu + \theta)}{\mu(\mu + q + \theta)}, \frac{\Lambda(\mu\rho + q)}{\mu(\mu + q + \theta)}, 0 \right)$.

Now we verify the conditions H1 and H2 as follows:

$$\frac{dX}{dt} = F(X,Z) = \begin{pmatrix} \frac{dS}{dt} = (1-\rho)\Lambda + \theta V + (1-\omega)\tau Q - (\lambda + q + \mu)S, \\ \frac{dV}{dt} = \rho\Lambda + qS - (\theta + (1-\pi)\lambda + \mu)V, \\ \frac{dR}{dt} = r_1 J - \mu R, \end{pmatrix} \qquad (2.55)$$

$$\frac{dX}{dt} = F(X,0) = \begin{pmatrix} \frac{dS}{dt} = (1-\rho)\Lambda + \theta V - (q + \mu)S \\ \frac{dV}{dt} = \rho\Lambda + qS - (\theta + \mu)V \\ \frac{dR}{dt} = 0 \end{pmatrix} \qquad (2.56)$$

Hence, X_0 is globally asymptotically stable meaning that the first condition $H1$ is satisfied.

For condition H2;

$$\frac{dZ}{dt} = G(X,Z) = \begin{pmatrix} \frac{dE}{dt} = \frac{\beta I(S + (1-\pi)V)}{N} + \frac{\beta\eta J(S + (1-\pi)V)}{N} - (p + \mu)E \\ \frac{dQ}{dt} = p\gamma E - (\tau + \mu)Q \\ \frac{dI}{dt} = p(1-\gamma)E - (\alpha + d_1 + \mu)I \\ \frac{dI}{dt} = \alpha I + \tau\omega Q - (r_1 + d_2 + \mu)J \end{pmatrix} \qquad (2.57)$$

From equation (2.57), it is clear that

$$G(X,O)=\begin{pmatrix}O\\O\\O\\O\end{pmatrix}=O.$$

Furthermore, $G(X,Z)=AZ-\hat{G}(X,Z)$, $\hat{G}(X,Z)=AZ-G(X,Z)$

With $A=D_Z(X_0,0)$ is an M-matrix (the off diagonal elements of A are nonnegative). Now let

$$\frac{dE}{dt}=G_1=\frac{\beta I(S+(1-\pi)V)}{N}+\frac{\beta\eta J(S+(1-\pi)V)}{N}-(p+\mu)E$$
$$\frac{dQ}{dt}=G_2=p\gamma E-(\tau+\mu)Q$$
$$\frac{dI}{dt}=G_3=p(1-\gamma)E-(\alpha+d_1+\mu)I$$
$$\frac{dI}{dt}=G_4=\alpha I+\tau\omega Q-(r_1+d_2+\mu)J$$

Therefore,

$$A=\begin{pmatrix}\frac{\partial G_1(E_0)}{\partial E} & \frac{\partial G_1(E_0)}{\partial Q} & \frac{\partial G_1(E_0)}{\partial I} & \frac{\partial G_1(E_0)}{\partial J}\\ \frac{\partial G_2(E_0)}{\partial E} & \frac{\partial G_2(E_0)}{\partial Q} & \frac{\partial G_2(E_0)}{\partial I} & \frac{\partial G_2(E_0)}{\partial J}\\ \frac{\partial G_3(E_0)}{\partial E} & \frac{\partial G_3(E_0)}{\partial Q} & \frac{\partial G_3(E_0)}{\partial I} & \frac{\partial G_3(E_0)}{\partial J}\\ \frac{\partial G_4(E_0)}{\partial E} & \frac{\partial G_4(E_0)}{\partial Q} & \frac{\partial G_4(E_0)}{\partial I} & \frac{\partial G_4(E_0)}{\partial J}\end{pmatrix}$$

$$A=\begin{pmatrix}-(p+\mu) & 0 & \beta & \eta\beta\\ p\gamma & -(\tau+\mu) & 0 & 0\\ p(1-\gamma) & 0 & -(\alpha+d_1+\mu) & 0\\ 0 & \tau\omega & \alpha & -(r_1+d_2+\mu)\end{pmatrix} \quad (2.58)$$

$$\hat{G}(X,Z)=AZ-G(X,Z)$$
$$=\begin{pmatrix}-(p+\mu) & 0 & \beta & \eta\beta\\ p\gamma & -(\tau+\mu) & 0 & 0\\ p(1-\gamma) & 0 & -(\alpha+d_1+\mu) & 0\\ 0 & \tau\omega & \alpha & -(r_1+d_2+\mu)\end{pmatrix}\begin{pmatrix}E\\Q\\I\\J\end{pmatrix}$$
$$-\begin{pmatrix}\frac{dE}{dt}=\frac{\beta I(S+(1-\pi)V)}{N}+\frac{\beta\eta J(S+(1-\pi)V)}{N}-(p+\mu)E\\ \frac{dQ}{dt}=p\gamma E-(\tau+\mu)Q\\ \frac{dI}{dt}=p(1-\gamma)E-(\alpha+d_1+\mu)I\\ \frac{dI}{dt}=\alpha I+\tau\omega Q-(r_1+d_2+\mu)J\end{pmatrix}$$

$$\hat{G}(X,Z)=\begin{pmatrix}\hat{G}_1(X,Z)\\ \hat{G}_2(X,Z)\\ \hat{G}_3(X,Z)\\ \hat{G}_4(X,Z)\end{pmatrix}=\begin{pmatrix}\beta I\left(1-\frac{S+(1-\pi)V}{N}\right)+\beta\eta J\left(1-\frac{S+(1-\pi)V}{N}\right)\\ 0\\ 0\\ 0\end{pmatrix}$$

2.59)

Since $\pi\in[0,1],\eta\in[0,1]$ and $0\le S+(1-\pi)V\le N$ then it is obvious that $\hat{G}(X,Z)\ge 0$. Hence, condition H2 is also satisfied. Thus, the disease free equilibrium of the model is globally asymptotically stable.

The Global Stability Analysis of the Endemic Equilibrium Point of the Model

Theorem 2.10:

The endemic equilibrium points of the model given by X_1, is globally asymptotically stable in the region Ω.

Proof:

Consider the following quadratic Lyapunov function with the following candidate:

$$W(S,V,E,Q,I,J,R)=\frac{1}{2}\left(S-S^*\right)^2+\frac{1}{2}\left(V-V^*\right)^2+\frac{1}{2}\left(E-E^*\right)^2+\frac{1}{2}\left(Q-Q^*\right)^2+\frac{1}{2}\left(I-I^*\right)^2+\frac{1}{2}\left(J-J^*\right)^2+\frac{1}{2}\left(R-R^*\right)^2 \quad (4.50)$$

Now differentiating equation (2.60) along the solution of the model equation given by system (2.1) gives

$$\frac{dW}{dt}=\left[\left(S-S^*\right)+\left(V-V^*\right)+\left(E-E^*\right)+\left(Q-Q^*\right)+\left(I-I^*\right)+\left(J-J^*\right)+\left(R-R^*\right)\right]\frac{d}{dt}\left[S+V+E+Q+I+J+R\right]\cdot \quad (2.61)$$

From system (2.1)

$$\frac{d}{dt}\left[S+V+E+I+J+R\right]=\Lambda-\mu\left[S+V+E+I+J+R\right]-d_1I-d_2J \quad (2.62)$$

Using equation (2.62) in equation (2.61)

$$\frac{dW}{dt}=\left[\left(S-S^{**}\right)+\left(V-V^*\right)+\left(E-E^*\right)+\left(Q-Q^*\right)+\left(I-I^*\right)+\left(J-J^*\right)+\left(R-R^*\right)\right]\times \left[\Lambda-\mu\left[S+V+E+Q+I+J+R\right]-d_1I-d_2J\right] \quad (2.63)$$

Now at steady state

$$\Lambda=\mu\left[S^*+V^*+E^*+Q^*+I^*+J^{**}+R^*\right]+d_1I^*+d_2J^* \quad (2.64)$$

Substituting equation (2.63) in equation (2.62) gives

$$\frac{dW}{dt}=\left[\left(S-S^{**}\right)+\left(V-V^*\right)+\left(E-E^*\right)+\left(Q-Q^*\right)+\left(I-I^*\right)+\left(J-J^*\right)+\left(R-R^*\right)\right]\times \left[\mu\left[S^*+V^*+E^*+Q^*+I^*+J^{**}+R^*\right]+d_1I^*+d_2J^*-\mu\left[S+V+E+Q+I+J+R\right]-d_1I-d_2J\right] \quad (2.65)$$

$$\frac{dW}{dt}=\left[\left(S-S^{**}\right)+\left(V-V^*\right)+\left(E-E^*\right)+\left(Q-Q^*\right)+\left(I-I^*\right)+\left(J-J^*\right)+\left(R-R^*\right)\right]\times \left[-\mu\left(S-S^{**}\right)-\mu\left(V-V^*\right)-\mu\left(E-E^*\right)-\mu\left(Q-Q^*\right)-\mu\left(I-I^*\right)-\mu\left(J-J^*\right)-\mu\left(R-R^*\right)-d_1\left(I-I^*\right)-d_2\left(J-J^*\right)\right] \quad (2.66)$$

After some series of expansions and simplifications;

$$\begin{aligned}\frac{dW}{dt}=&-\left(S-S^*\right)\left[\mu\left[\left(S-S^*\right)+\mathrm{H}_1\right]+\mathrm{M}\right]-\left(V-V^*\right)\left[\mu\left[\left(V-V^*\right)+\mathrm{H}_2\right]+\mathrm{M}\right]\\&-\left(E-E^*\right)\left[\mu\left[\left(E-E^*\right)+\mathrm{H}_3\right]+\mathrm{M}\right]-\left(Q-Q^*\right)\left[\mu\left[\left(Q-Q^*\right)+\mathrm{H}_4\right]+\mathrm{M}\right]\\&-\left(I-I^*\right)\left[\mu\left[\left(I-I^*\right)+\mathrm{H}_5\right]+\mathrm{M}\right]-\left(J-J^*\right)\left[\mu\left[\left(J-J^*\right)+\mathrm{M}_6\right]+\mathrm{M}\right]\\&-\left(R-R^*\right)\left[\mu\left[\left(R-R^*\right)+\mathrm{M}_7\right]+\mathrm{H}\right]\end{aligned} \quad (2.67)$$

where

$$H_1 = (V - V^*) + (E - E^*) + (Q - Q^*) + (I - I^*) + (J - J^*) + (R - R^*),$$
$$H_2 = (S - S^*) + (E - E^*) + (Q - Q^*) + (I - I^*) + (J - J^*) + (R - R^*),$$
$$H_3 = (S - S^*) + (V - V^*) + (Q - Q^*) + (I - I^*) + (J - J^*) + (R - R^*),$$
$$H_4 = (S - S^*) + (V - V^*) + (E - E^*) + (I - I^*) + (J - J^*) + (R - R^*),$$
$$H_5 = (S - S^*) + (V - V^*) + (Q - Q^*) + (E - E^*) + (J - J^*) + (R - R^*),$$
$$H_6 = (S - S^*) + (V - V^*) + (Q - Q^*) + (E - E^*) + (I - I^*) + (R - R^*),$$
$$H_7 = (S - S^*) + (V - V^*) + (Q - Q^*) + (E - E^*) + (I - I^*) + (J - J^*),$$
$$M = d_1 (I - I^*) + d_2 (J - J^*).$$

From equation (2.67) it is clear that $\frac{dW}{dt} \leq 0$ and $\frac{dW}{dt} = 0$ if and only if $S = S^*, V = V^*, E = E^*, Q = Q^*, I = I^*, J = J^*, R = R^*$. Furthermore, every solution of the model equation given by system (2.1) approaches the endemic equilibrium point, (X_1) as $t \to \infty$. Hence, the largest positively invariant set in $\left\{(S, V, E, Q, I, J, R) \in \Omega : \frac{dW}{dt} = 0\right\}$ is the singleton (X_1). Hence, according to the Lassalle's invariance principle the endemic equilibrium point of the model is globally asymptotically stable in the region Ω.

Sensitivity Analysis on (R_0)

To determine how best to reduce human mortality and morbidity due to TB, it is necessary to know the relative performance of different factors responsible for its transmission and prevalence. Knowing that disease transmission is directly related to the reproduction number (R_0), the sensitivity indices of the model parameters are calculated with respect to the reproduction number. These indices tell us how important each parameter is with respect to disease transmission and control. The essence of sensitivity analysis is to determine the robustness of model predictions to parameters and to discover which parameters have a high impact on the reproduction number. Following Chitnis et al., (2008), an analytical expression for the sensitivity to each parameter with respect to the reproduction number is driven.

$$Z_{\rho}^{R_0} = \frac{\partial R_0}{\partial \rho} \times \frac{\rho}{R_0} \qquad (2.69)$$

Applying this formula using the reproduction number R_0 and the values of the parameters in Table (3), the sensitivity indices of the model parameters with respect to the reproduction number and the result are presented in Table (4).

Table 3: Parameter values for sensitivity analysis

parameter	Value	Reference
ρ	0.8	Estimated
d_2	0.4	Estimated
α	0.8	Estimated
β	0.35	Agusto, 2009
ω	0.2	Estimated
γ	0.6	Estimated
P	0.03	Nyerere, *et al.*, 2014
μ	0.2	Andreir, 2007
η	0.3	Estimated
π	0.8	Nyerere, *et al.*, 2014
θ	0.7	Estimated
r_1	0.9	Estimated
d_1	0.4	Adetunde, 2007
τ	0.2	Estimated

A positive index indicate that the value of R_0 increases as the parameter is increased while a negative index means the value of R_0 decreases as the parameters is increased.

Table 4: Sensitivity indices

Parameter	Sensitivity index
ρ	-0.2036
d_2	-0.0504
α	-0.3878
β	1.0000
ω	0.0419
γ	-1.3952
P	0.8772
μ	-1.1919
η	0.2016
π	-0.2341
r_1	-0.1176
d_1	-0.2737
q	-0.1309

From Table (4), it is observed that increase (or decrease) in the value of the parameter (β), the per capita transmission, increases (or decreases) the reproduction number by 10%. Increase (or decreasing) in the value of the quarantine parameter (ω), increases (or decreases) the reproduction number by 0.4%. Increase (or decrease) of proportion of exposed individuals to infected class (p), increases (or decreases) the reproduction number by 8.7%. Increase (or decrease) of value of probability of acquiring TB (η), increases (or decreases) the reproduction number by 0.2%. Also, increasing (or decreasing) the rate of diagnosis (τ), increases (or decreases) the reproduction number by 0.2%. Increasing (or decreasing) rate of vaccination at birth (θ), increases (or decreases) the reproduction number by 2.5%. In the same manner the negative sign of the sensitivity index of R_0 means an inverse relationship between these parameters and R_0. The relationship implies increase (or decrease) in expose to quarantine (γ) leads to approximately a 13.9% decrease (or increase) in R_0. Likewise increase (or decrease) in TB induce death (d_2) leads to approximately a 0.5% decrease (or increase) in R_0 increase (or decrease) in (α) rate of infected individuals goes for treatment and (μ) natural death leads to approximately 3.8% and 11.9% decrease (or increase) in R_0 respectively. Similarly increase (or decrease) in recovery rate (r_1) leads to approximately1.1% decrease (or increase) in R_0. Similarly, increase (or decrease) in TB induce rate for infected individuals (d_1) leads to approximately a 2.7 % decrease (or increase) in R_0 .Also increase (or decrease) in efficacy of vaccination (π) leads to approximately a 2.3% decrease (or increase) in R_0. Also, increase (or decrease) in proportion of vaccination (ρ) leads to approximately a 2.0% decrease (or increase) in R_0 .Increase (or decrease) in rate of vaccine of susceptible individuals (q) leads to approximately a 1.3 % decrease (or increase) in R_0. In conclusion, the per capital transmission rate from susceptible individuals to expose class (β) has the highest positive sensitivity index value β=1.0000 and the expose individuals to quarantine (γ) has the highest negative sensitivity index with value γ= - 1.3952

Conclusion

(i) Extension of the Model
(ii) The existence, positivity, and bounded ness of the solution of the autonomous model were investigated, and the results have shown that the model is epidemiologically feasible and mathematically well-posed in the particular domain.

(iii) The autonomous model has two equilibrium points, namely, the disease free and the endemic equilibrium points.
(iv) The basic reproduction number was determined.
(v) The stability analyses of the equilibrium points of the model were studied, and the results revealed that both the disease free and the endemic equilibrium points are globally asymptotically stable.
(vi) A sensitivity analysis of the model parameters with respect to the basic reproduction number was carried out. The results have shown that some parameters, such as contact rate, have a positive impact on the reproduction number, while others, such as TB-induced death rate, have a negative impact on the reproduction number.

Recommendations

i. Proper education and sensitization on TB should be given to the general public by the government and non-governmental organizations (NGO).
ii. Government at national, state, local level should create an awareness program for early diagnoses of TB disease.
iii. Health care workers should ensure that patients have completed their treatments.

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