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Modeling the Effect of Stress and Stigma on the Transmission and Control of Tuberculosis Infection

Lalashe Lengiteng'i[a*], Damian Kajunguri[b],Yaw Nkansah-Gyekye[c]

[a,b,c]*The Nelson Mandela African Institution of Science and Technology, P.O.Box 447, Arusha, Tanzania*

[a]*Email: lengiteng'il@nm-aist.ac.tz*

[b]*Email: damian.kajunguri@nm-aist.ac.tz*

[c]*Email: yaw.nkansah-gyekye@nm-aist.ac.tz*

Abstract

In this paper a continuous time deterministic model with health education campaign and treatment strategy is formulated to assess the effect of stress and stigma on the transmission and control of Tuberculosis (TB). The effective reproduction number $\Re_e$ is obtained and used to investigate the impact of health education campaign and treatment strategies. The effective reproduction numbers for health education campaign and treatment considered separately were found not to be effective as compared to a combination of both strategies. Numerical simulation results show that TB can be reduced or eliminated from the community when $\Re_0 < 1$ as treatment is applied. The disease prevalence and incidence are high when stigma is high and decline gradually when the combination of both treatment and health campaign are administered. We recommend that health education campaign to reduce stress among individuals and stigma for infectious individuals should be accompanied by treatment of active TB individuals for improved reduction of TB disease.

Keywords: Tuberculosis; Stress; Stigma; Effective reproduction number; simulations.

1. Introduction

Tuberculosis (TB) is bacteria infectious disease caused by pathogen *Mycobacterium tuberculosis* with more than one-third of the world human population as its reservoir [4, 13, 15].

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* Corresponding author.

Global annual estimates of 8.6 million people develop tuberculosis, of which 1.3 million die from to disease. It is estimated in [13] that, the burden of disease caused by TB is high in developing countries where poor nutrition, congested accommodation and emergence of HIV are manifested. The global estimates of incidence, prevalence and mortality rates per 100000 human populations in 2012 were respectively 255, 303 and 26 and Tanzania incidence, prevalence and mortality rates per 100000 human population were 165, 176 and 13 respectively [23]. Tuberculosis disease is mainly of two types: pulmonary and extra-pulmonary tuberculosis. Pulmonary tuberculosis is the common form of TB that affects lung while extra-pulmonary TB affects other parts of the body and organs including central nervous system and bones [22].

This study focuses on pulmonary TB. Tuberculosis is an epidemic disease spreading in the air when the infectious person with pulmonary TB expel bacteria by coughing, singing, sneezing, speaking, spiting and so on [7]. It is estimated that a small proportion of about 10% of infected individuals with *Mycobacterium tuberculosis* develop TB and become infectious within two years upon infected [18]. Most become latent for the rest of their lives as long as their immune system is not compromised [7]. The recovered individuals from TB do not acquire permanent immunity, some of them they become latent again. However, the emergence of TB stigma for infected individuals and stress in the population adhered the effectiveness of TB treatment strategies. Stigma is a process by which the reaction of others spoils normal identities. The major cause of TB stigma is the perceived risk of transmission from TB infected individuals to susceptible community members.

Depending on geographical region, however, TB is stigmatized because of its association with HIV, poverty, low social class, malnution, or disreputable behaviour [7, 8]. TB patients perceive themselves to be at risk for a number of stigma-related social and economic consequences. Because the most common result of tuberculosis stigma is isolation from other members of the community, TB infections can substantially impact economic opportunities [8]. When an individual die of TB, fear of TB stigma can lead families to hide the cause of death to other members of the community, even when such information might be useful in targeted TB screening [8]. Similarly, fear of TB stigma can leads TB infected individuals to hide their TB status from the family members [8]. TB stigma also results in a sense of shame or guilt leading to self-isolation as TB infected individuals internalize their community's negative judgments about the disease [15]. Lack of knowledge regarding routes of TB transmission may also contribute to TB stigma [13]. Some TB patients fear losing their jobs [14], thus, they develop TB stigma.

Mathematical modeling of epidemiology of Tuberculosis has recently become the powerful tool to study the dynamics of the disease and importance of various control strategies in order to advice public health policy makers to construct suitable interventions programs to combat TB infections. However, there is no rigorous mathematical model that addressed the impact of stigma in controlling the TB dynamics.

This study concentrate on developing a TB model with stigma education campaign and treatment strategies in order to investigate the effects of both stress and stigma on TB transmission dynamics of population that is purely homogeneous. To assess clearly the effect of stigma on the dynamics of TB, we subdivide the infectious class into infectious without stigma I_1 and stigmatized infectious I_2 in order to assess clearly the effect of stigma on TB treatment strategies.

2. Model Formulation

The proposed model is subdivided into five compartments and developed from the basic $SLIR$ (Susceptible-Exposed-Infectious-Recovered) compartments model. A compartment of stigmatized infectious I_2 is added to form SLI_1I_2R model. Stigmatized infectious class isolate themselves from infectious class I_1 due to TB stigma. In this model susceptible population will be recruited at a rate Λ. Susceptible individuals come into contact with infectious individuals and get infected at a rate (force of infection) of $\lambda = \frac{c\beta(I_1 + I_2)}{N}$.

After infection, a proportion p undergo fast progression to active TB, and the remaining proportion $(1-p)$ undergo slow progression to latently infected class. Individuals who undergo fast and slow progression are affected with a stress enhancement factor α_5 and α_1 respectively. Latently infected individuals progress to active TB at a rate δ and stress factor α_2. The unstigmatized infectious individuals recover naturally from the disease at a rate τ. After treatment, the unstigmatized infectious individuals are assumed to recover at a rate δ_1. Infectious individuals in class I_1 progress to the stigmatized class I_2 at a rate q. This is affected by the stigma factor η and stress factor α_3. The recovered individuals are assumed to move back to infectious class at a rate of ϕ due to exogenous re-infection and stress factor α_4. We assume that when TB stigma reduction education campaign ε is administered the proportion φ of stigmatized infectious individuals reverts back to unstigmatized infectious class and the remaining proportion $(1-\varphi)$ progresses to recovered class at a rate ϕ_2. The infectious individuals, I_1 and I_2 are assumed to have additional constant disease induced mortality rate d while the rest die naturally at a rate of μ. All variables and parameters are assumed to be TB non-negative.

In addition the following assumptions are taken into consideration during the formulation of the model:

i. We assume that stigma affect only the infectious classes.
ii. All individuals are born susceptible.
iii. The members of population mix homogeneously.
iv. All population is affected by stress at different levels.
v. Once recovered from treatments an individual reverts to the latent and may experience other episode of disease.
vi. All population except infectious population has equal death rate μ.
vii. The TB mortality rate is the same for both TB infectious and stigmatized TB infectious.
viii. We assume that all recruits, that is, newborns and immigrants, are neither immune nor infected.
ix. If an individual is infected he/she will become infectious and can develop active TB disease if not

treated.

The description of model formulation in section 2, together with the assumptions above leads to compartmental diagram in Figure 1.

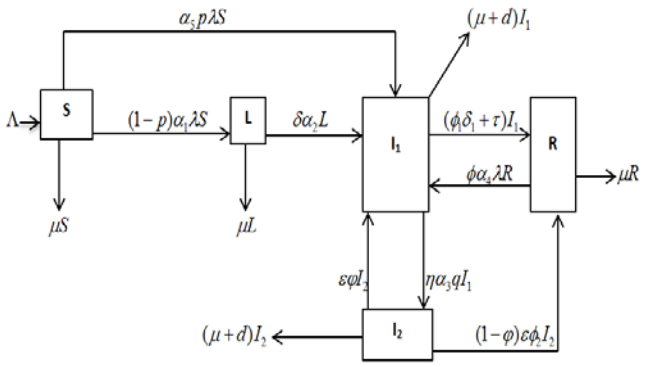

Figure 1: Schematic flow diagram showing dynamics of tuberculosis.

The full description of variables and parameters used to formulate the model are in Table 1 and Table 2 respectively:

Table 1: Description of variables of the model.

Variable	Description
$S(t)$	The susceptible who are at risk of being infected at time t.
$L(t)$	The latently infected individuals at time t.
$I_1(t)$	Individuals who are infectious at time t.
$I_2(t)$	Infectious individuals who are stigmatized at time t.
$R(t)$	Individuals treated (Recovered) against TB at time t.

Basing on assumptions made and relationship that exists between variables shown in Figure 1, the system of five ordinary differential equations that describes the impact of stress and stigma on the dynamics of TB infections following the idea of [2] is given by:

$$\frac{dS}{dt} = \Lambda - \alpha_5 p\lambda S - (1-p)\alpha_1\lambda S - \mu S,$$

$$\frac{dL}{dt} = (1-p)\alpha_1\lambda S - \delta\alpha_2 L - \mu L,$$

$$\frac{dI_1}{dt} = \alpha_5 p\lambda S + \delta\alpha_2 L + \varepsilon\varphi I_2 + \phi\alpha_4\lambda R - \left(d + \mu + (\phi_1\delta_1 + \tau) + q\eta\alpha_3\right)I_1, \qquad (1)$$

$$\frac{dI_2}{dt} = q\eta\alpha_3 I_1 - \left(\varepsilon\varphi + d + \mu + (1-\varphi)\varepsilon\phi_2\right)I_2,$$

$$\frac{dR}{dt} = (\phi_1\delta_1 + \tau)I_1 + (1-\varphi)\varepsilon\phi_2 I_2 - \left(\phi\alpha_4\lambda + \mu\right)R.$$

Table 2: Description of Parameters of the model.

Parameter	Description
Λ	Recruitment rate of the population.
β	Transmission rate.
c	Per capita contact rate.
μ	Per capita natural mortality death rate.
d	Per capita death rate due to TB disease.
δ	Progression rate of disease to active TB.
α_1	Stress factor for slow progression from S to L.
α_2	Enhancement stress factor for re-infection (exogenous reactivation).
α_3	Stress factor for progression from I_1 to I_2.
α_4	Stress factor for progression from R to I_1.
α_5	Stress factor for fast progression.
φ	The proportion of stigmatized infectious who return back to unstigmatized infectious after TB stigma education campaign.
ϕ_1	Recovery rate of infectious class.
ϕ_2	Recovery rate of stigmatized TB infectious.
η	The rate of stigmatization.
q	The rate of progression from I_1 to I_2.
τ	The rate of unstigmatized infectious who recover naturally.
δ_1	The rate of treatment for unstigmatized infectious individuals.
p	Proportion of susceptible who progress fast to infectious enhanced by the stress factor α_5.
ϕ	The rate of re-infection.
ε	The rate of education campaign on controlling TB stigma.

By adding the state equations in (1) we end up with rate of change of population,

$$\frac{dN}{dt} = \Lambda - \mu N - \mu L - \left(\varepsilon\varphi + d + \mu - (\phi_1\delta_1 + \tau)\right)I_1 - (d+\mu)I_2,$$

where

$$\lambda = \frac{c\beta(I_1 + I_2)}{N}.$$

3. Model analysis

The model system (1) is analyzed qualitatively to get the insight into its dynamical features which gives better understanding of the impact of stress and stigma on the dynamics and treatment strategies of TB infections.

3.1 Existence of Disease Free Equilibrium (DFE)

We obtain the disease free equilibrium point (DFE) by setting the right hand side of system (1) equal to zero.

That is:

$$\frac{dS}{dt} = \frac{dL}{dt} = \frac{dI_1}{dt} = \frac{dI_2}{dt} = \frac{dR}{dt} = 0. \qquad (2)$$

Let the disease free equilibrium (DFE) of tuberculosis model (1) be $E_0 = \left(S^0, L^0, {I_1}^0, {I_2}^0, R^0\right)$ and in the absence of the disease we set $L = I_1 = I_2 = R = 0,$ we found that,

$$E_0 = \left(S^0, L^0, {I_1}^0, {I_2}^0, R^0\right) = \left(\frac{\Lambda}{\alpha_5 p + \mu}, 0, 0, 0, 0\right). \qquad (3)$$

3.2 Effective Reproduction Number, $\Re_e$

The basic reproduction number denoted by $\Re_0$ is the average number of secondary infections caused by an infectious individual during his/her entire period of infectiousness [27, 29]. The basic reproduction number is an important non-dimensional quantity in epidemiology as it sets the threshold in the study of the disease both for predicting its outbreak and for evaluating its control strategies. Further, stability of equilibria can be analyzed using $\Re_0$. If $\Re_0 < 1$ it means that every infectious individual will cause less than one secondary infection and hence the disease will die out and when $\Re_0 > 1,$ every infectious individuals will cause more than one secondary infection and hence the disease will invide the population. In our model, we compute the basic

reproduction number using the next generation approach [27]. The basic reproduction number is obtained by taking the largest (dominant) eigenvalues (spectral radius) of

$$FV^{-1} = \left[\frac{\partial F_i}{\partial x_i}(E_0)\right]\left[\frac{\partial V_i}{\partial x_i}(E_0)\right]^{-1} \tag{4}$$

where F_i the rate of appearance of new infection in compartment i, V_i the transfer of infections from one compartment to another and E_0 is the disease free equilibrium. From system (1) we re-write the equation with infection cases L, I_1, and I_2 which leads to the system (5) below:

$$\begin{aligned}
\frac{dL}{dt} &= (1-p)\alpha_1\lambda S - \delta\alpha_2 L - \mu L,\\
\frac{dI_1}{dt} &= \alpha_5 p\lambda S + \delta\alpha_2 L + \varepsilon\varphi I_2 + \phi\alpha_4\lambda R - \left(d + \mu + (\phi_1\delta_1 + \tau) + q\eta\alpha_3\right)I_1,\\
\frac{dI_2}{dt} &= q\eta\alpha_3 I_1 - \left(\varepsilon\varphi + d + \mu + (1-\varphi)\varepsilon\phi_2\right)I_2.
\end{aligned} \tag{5}$$

From system (5),

$$F_i = \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} (1-p)\alpha_1\lambda S \\ \alpha_5 p\lambda S \\ 0 \end{bmatrix},$$

where,

$$\lambda = \frac{c\beta(I_1 + I_2)}{N}.$$

Partial differentiation of F_i with respect to L, I_1, and I_2 at DFE (E_0),

$$F = \begin{bmatrix} \frac{\partial F_1}{\partial L}(E_0) & \frac{\partial F_1}{\partial I_1}(E_0) & \frac{\partial F_1}{\partial I_2}(E_0) \\ \frac{\partial F_2}{\partial L}(E_0) & \frac{\partial F_2}{\partial I_1}(E_0) & \frac{\partial F_2}{\partial I_2}(E_0) \\ \frac{\partial F_3}{\partial L}(E_0) & \frac{\partial F_3}{\partial I_1}(E_0) & \frac{\partial F_2}{\partial I_2}(E_0) \end{bmatrix},$$

This gives,

$$F = \begin{bmatrix} 0 & (1-p)c\beta & (1-p)c\beta \\ 0 & \alpha_5 pc\beta & \alpha_5 pc\beta \\ 0 & 0 & 0 \end{bmatrix}.$$

On the other hand,

$$V_i = \begin{bmatrix} (\delta\alpha_2 + \mu)L \\ -\delta\alpha_2 L - \varepsilon\varphi I_2 - \phi\alpha_4\lambda R + (d + \mu + (\phi_1\delta_1 + \tau) + \eta q\alpha_3)I_1 \\ -q\eta\alpha_3 I_1 + (\varepsilon\varphi + d + \mu + (1-\varphi)\varepsilon\phi_2)I_2 \end{bmatrix},$$

Partial differentiation of V_i with respect to $L, I_1,$ and I_2 at DFE (E_0),

$$V = \begin{bmatrix} \frac{\partial V_1}{\partial L}(E_0) & \frac{\partial V_1}{\partial I_1}(E_0) & \frac{\partial V_1}{\partial I_2}(E_0) \\ \frac{\partial V_2}{\partial L}(E_0) & \frac{\partial V_2}{\partial I_1}(E_0) & \frac{\partial V_2}{\partial I_2}(E_0) \\ \frac{\partial V_3}{\partial L}(E_0) & \frac{\partial V_3}{\partial I_1}(E_0) & \frac{\partial V_2}{\partial I_2}(E_0) \end{bmatrix},$$

This gives,

$$V = \begin{bmatrix} a & 0 & 0 \\ -\delta\alpha_2 & b & -\varepsilon\varphi \\ 0 & -q\eta\alpha_3 & c \end{bmatrix},$$

where $a = \delta\alpha_2 + \mu$, $b = d + \mu + (\phi_1\delta_1 + \tau) + \eta q\alpha_3$, and $c = \varepsilon\varphi + d + \mu + (1-\varphi)\varepsilon\phi_2$. Then, the inverse of V and product matrix FV^{-1} are computed and respectively found to be:

$$V^{-1} = \begin{bmatrix} \frac{1}{a} & 0 & 0 \\ \frac{\delta\alpha_2 c}{a(bc - \varepsilon\varphi q\eta\alpha_3)} & \frac{c}{bc - \varepsilon\varphi q\eta\alpha_3} & \frac{\varepsilon\varphi}{bc - \varepsilon\varphi q\eta\alpha_3} \\ \frac{\delta\alpha_2 q\eta\alpha_3}{a(bc - \varepsilon\varphi q\eta\alpha_3)} & \frac{q\eta\alpha_3}{bc - \varepsilon\varphi q\eta\alpha_3} & \frac{b}{bc - \varepsilon\varphi q\eta\alpha_3} \end{bmatrix},$$

and

$$FV^{-1} = \begin{bmatrix} \dfrac{(1-p)c\beta\alpha_2(c+q\eta\alpha_3)}{a(bc-\varepsilon\varphi q\eta\alpha_3)} & \dfrac{(1-p)c\beta(c+q\eta\alpha_3)}{bc-\varepsilon\varphi q\eta\alpha_3} & \dfrac{(1-p)c\beta(\varepsilon\varphi+b)}{bc-\varepsilon\varphi q\eta\alpha_3} \\ \dfrac{\alpha_2\alpha_5 p\delta c\beta(c+q\eta\alpha_3)}{a(bc-\varepsilon\varphi q\eta\alpha_3)} & \dfrac{\alpha_5 qc\beta(c+q\eta\alpha_3)}{bc-\varepsilon\varphi q\eta\alpha_3} & \dfrac{\alpha_5 qc\beta(\varepsilon\varphi+b)}{bc-\varepsilon\varphi q\eta\alpha_3} \\ 0 & 0 & 0 \end{bmatrix}.$$

The eigenvalues of matrix product FV^{-1} are $0,\ 0,$ and $c\beta\left[\dfrac{(\delta(1-p)\alpha_2+\alpha_5 ap)(c+q\eta\alpha_3)}{a(bc-\varepsilon\varphi q\eta\alpha_3)}\right].$

Thus, the effective reproduction number is:

$$\Re_e = c\beta\left[\frac{(\delta(1-p)\alpha_2+\alpha_5 ap)(c+q\eta\alpha_3)}{a(bc-\varepsilon\varphi q\eta\alpha_3)}\right].$$

Substituting for $a, b,$ and $c,$ we obtain the effective reproduction number:

$$\Re_e = c\beta\left[\frac{(\delta(1-p)\alpha_2+\alpha_5 p(\delta\alpha_2+\mu))(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2+q\eta\alpha_3)}{(\delta\alpha_2+\mu)[(d+\mu+(\phi_1\delta_1+\tau)+\eta q\alpha_3)(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2)-\varepsilon\varphi q\eta\alpha_3]}\right]. \quad (6)$$

When there is no control strategies we have $\phi_1 = \phi_2 = \varepsilon = 0.$ Thus, the basic reproduction number for the system (1) is,

$$\Re_0 = c\beta\left[\frac{(\delta\alpha_2(1-p)+\alpha_5 p(\delta\alpha_2+\mu))(d+\mu+q\eta\alpha_3)}{(\delta\alpha_2+\mu)((d+\mu+\tau+q\eta\alpha_3)(d+\mu))}\right]. \quad (7)$$

3.3. Analysis of Effective Reproduction Number with Unique Control Strategies

In this section, we use the effective reproduction number in equation (6) to compute the reproduction numbers for individual control strategies as in [13, 14, 15].

If treatment is the only control strategy that is $\phi_1 \neq 0, \phi_2 \neq 0, \varepsilon = 0,$ then the basic reproduction number with treatment only, $\Re_{e1}$ is given by:

$$\Re_{e1} = c\beta\left[\frac{\left(\delta\alpha_2(1-p)+\alpha_5 p(\delta\alpha_2+\mu)\right)\left(d+\mu+\varepsilon\phi_2+q\eta\alpha_3\right)}{\left(\delta\alpha_2+\mu\right)\left(d+\mu+(\phi_1\delta_1+\tau)+\eta q\alpha_3\right)\left(d+\mu+\varepsilon\phi_2\right)}\right]. \quad (8)$$

When there is no treatment and education campaign is only employed as control strategy we have $\phi_1 = \phi_2 = 0, \varepsilon \neq 0,$ the basic reproduction number with education only, $\Re_{e2}$ is given by:

$$\Re_{e2} = c\beta\left[\frac{\left(\delta\alpha_2(1-p)+\alpha_5 p(\delta\alpha_2+\mu)\right)\left(\varepsilon\varphi+d+\mu+q\eta\alpha_3\right)}{\left(\delta\alpha_2+\mu\right)\left(d+\mu+\tau+q\eta\alpha_3\right)\left(\varepsilon\varphi+d+\mu-\varepsilon\varphi\eta q\alpha_3\right)}\right]. \quad (9)$$

3.4 Analysis of the Effective Reproduction Number with Stress and Stigma separately

In this section, we analyse the effective reproduction number to gain insight on the impact of stress and stigma separately on the dynamics of the disease with control strategies. The similar approach was done by [13, 14, 15, 22].

When there is no stress that is $\alpha_i\,(i=1,2,3,4,5)=1, \eta \neq 1$ the effective reproduction number with stigma only, $\Re_{e4}$ is given by:

$$\Re_{e4} = c\beta\left[\frac{\left(\delta(1-p)+p(\delta+\mu)\right)\left(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2+\eta q\right)}{\left(\delta+\mu\right)\left(d+\mu+(\phi_1\delta_1+\tau)+\eta q\right)\left(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2-\varepsilon\varphi q\eta\right)}\right]. \quad (10)$$

When there is no stigma that is $\alpha_i\,(i=1,2,3,4) \neq 1, \eta = 1,$ the effective reproduction number with stress, $\Re_{e3}$ is given by:

$$\Re_{e3} = c\beta\left[\frac{\left(\delta\alpha_2(1-p)+\alpha_5 p(\delta\alpha_2+\mu)\right)\left(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2\right)}{\left(\delta\alpha_2+\mu\right)\left(d+\mu+(\phi_1\delta_1+\tau)\right)\left(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2\right)}\right]. \quad (11)$$

3.4. Local Stability of the Disease-Free Equilibrium (DFE)

Theorem 1: *The disease free equilibrium of model (1) is locally asymptotically stable if* $\Re_e < 1$ *and unstable if* $\Re_e > 1.$

We prove theorem 1 for local stability of DFE by asserting that the trace and determinant of Jacobian matrix at DFE denoted by J_{E_0} are strictly negative and positive respectively. The Jacobian matrix evaluated at DFE point is given by:

$$J_{E_0}=\begin{bmatrix} -(\alpha_5 p+\mu) & 0 & (1-p)\alpha_1 c\beta & (1-p)\alpha_1 c\beta & 0 \\ 0 & -(\delta\alpha_2+\mu) & (1-p)\alpha_1 c\beta & (1-p)\alpha_1 c\beta & 0 \\ 0 & \delta\alpha_2 & \alpha_5 pc\beta-(d+\mu+(\phi_1\delta_1+\tau)_1+q\eta\alpha_3) & \alpha_5 pc\beta+\varepsilon\varphi & 0 \\ 0 & 0 & q\eta\alpha_3 & -(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2) & 0 \\ 0 & 0 & (\phi_1\delta_1+\tau) & (1-\varphi)\varepsilon\phi_2 & -\mu \end{bmatrix}.$$

Trace and determinant of matrix $J(E_0)$ denoted by $Tr(J(E_0))$ and $\det(J(E_0))$ are respectively given by:

$$Tr(J(E_0))=-(e_1+e_7+\mu-(e_4+e_5)), \tag{11a}$$

and

$$\det(J(E_0))=e_1\mu(\delta\alpha_2(e_2e_7+q\eta\alpha_3e_3)-e_4(e_7e_5+q\eta\alpha_3+e_6)), \tag{11b}$$

where $e_1=\alpha_5 p+\mu,\quad e_2=e_3=(1-p)\alpha_1 c\beta,\quad e_5=\alpha_5 pc\beta-(e_4+\mu+(\phi_1\delta_1+\tau)+q\eta\alpha_3),$ $e_6=\alpha_5 pc\beta+\varepsilon\varphi,$ and $e_7=\varepsilon\varphi+e_4+\mu+(1-q)\varphi\phi_2.$

Thus $\det(J(E_0))>0$ if and only if $\delta\alpha_2(e_2e_7+q\eta\alpha_3e_3)>e_4(e_7e_5+q\eta\alpha_3e_6)$ and $Tr(J(E_0))<0$ if and only if $e_1+e_7+\mu>e_4+e_5$, then the disease free equilibrium point E_0 is locally asymptotically stable.

3.5. Global Stability of Disease-Free Equilibrium Point with Control

We analyze the global stability of disease free equilibrium point of model (1) by using an approach presented in [5, 18, 21, 30]. The model (1) can be written in the following format:

$$\begin{aligned} \frac{dX_n}{dt}&=A(X_n-X_{DFE})+A_1X_i, \\ \frac{dX_i}{dt}&=A_2X_i. \end{aligned} \tag{11ba}$$

From (11ba), X_n and X_i are vectors of no transmitting and transmitting compartments respectively. X_{DFE} is the vector at disease free equilibrium point (DFE) of the same length as X_n. From model (1) we define:

$$X_n=(S,R)^T,\ X_i=(L,I_1,I_2)^T,\ X_{DFE}=\left(\frac{1}{\alpha_5 p+\mu},0\right)^T,\text{ and }\ X_n-X_{DFE}=\begin{pmatrix} S-\dfrac{1}{\alpha_5 p+\mu} \\ R \end{pmatrix}.$$

For global stability of DFE we need to show that matrix A has real negative eigenvalues and A_2 is a Metzler

matrix (i.e the off-diagonal elements of A_2 are non-negative, symbolically denoted by $A_2\left(X_{ij}\right)\geq 0, \forall_i \neq j$). Using system (1), then the first and second equations in (11ba) can be written respectively in expanded form as:

$$\begin{pmatrix} \Lambda-(\alpha_5 p\lambda+(1-p)\alpha_1\lambda+\mu)S \\ \phi_1 I_1+(1-\varphi)\varepsilon\phi_2 I_2-(\phi\alpha_4\lambda+\mu)R \end{pmatrix}=A\begin{pmatrix} S-\dfrac{1}{\alpha_5 p+\mu} \\ R \end{pmatrix}+A_1\begin{pmatrix} L \\ I_1 \\ I_2 \end{pmatrix},$$

and $$\begin{pmatrix} (1-p)\alpha_1\lambda S-(\delta\alpha_2+\mu)L \\ \alpha_5 p\lambda S+\delta\alpha_2 L+\varepsilon\varphi I_2+\phi\alpha_4\lambda R-(d+\mu+(\phi_1\delta_1+\tau)+q\eta\alpha_3)I_1 \\ q\eta\alpha_3 I_1-\left(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon(\phi_1\delta_1+\tau)\right)I_2 \end{pmatrix}=A_2\begin{pmatrix} L \\ I_1 \\ I_2 \end{pmatrix}.$$

For compatibility, matrices A, A_1 and A_2 should be order 2×2 and 3×3 respectively. By using non-transmitting elements from Jacobian matrix of system (1) and representing in (11ba) we found that:

$$A=\begin{pmatrix} -\mu & 0 \\ 0 & -\mu \end{pmatrix},$$

$$A_1=\begin{pmatrix} -\left(\alpha_5 p+(1-p)\alpha_1\right)c\beta s & -\left(\alpha_5 p+(1-p)\alpha_1\right)c\beta s \\ (\phi_1\delta_1+\tau)+\phi\alpha_4 c\beta R & (1-\varphi)\varepsilon\phi_2-\phi\alpha_4 c\beta R \end{pmatrix},$$

and

$$A_2=\begin{pmatrix} -\left(\delta\alpha_2+\mu\right) & (1-p)\alpha_1 c\beta\dfrac{S}{N} & (1-p)\alpha_1 c\beta\dfrac{S}{N} \\ \delta\alpha_2 & -(\chi_1+\chi_2+\chi_3) & \alpha_5 pc\beta\dfrac{S}{N}+\phi\alpha_4 c\beta\dfrac{S}{N}+\varepsilon\varphi \\ 0 & q\eta\alpha_3 & -(\varepsilon\varphi+d+\mu+(1-\varphi)\varepsilon\phi_2) \end{pmatrix},$$

where $\chi_1=(d+\mu+(\phi_1\delta_1+\tau)+q\eta\alpha_3)\dfrac{S}{N}$, $\chi_2=(\alpha_5 pc\beta+\phi\alpha_4 c\beta)\dfrac{S}{N}$,

$\chi_3=\alpha_5 pc\beta\dfrac{S}{N}+\phi\alpha_4 c\beta\dfrac{S}{N}+(d+\mu+(\phi_1\delta_1+\tau)+q\eta\alpha_3)$. We found that A is upper triangular matrix whose eigenvalues are located on its main diagonal. Therefore eigenvalues of A (i.e $-\mu$ and $-\mu$) are real and distict and negative. In addition A_2 is a Metzler matrix since its off diagonal matrix is non-negative if and only if $(1-p)>0$. That is $0\leq L, I_1, I_2, R<1$. Therefore, DFE of system (1) is globally asymptotically stable. We have established important theorem.

Theorem 2: *The disease-free equilibrium point is globally asymptotically stable if* $\Re_e < 1.$ *and unstable if* $\Re_e > 1.$

3.6. Global Stability of Endemic Equilibrium Point of a Model with Control

In this section, we prove the global stability of endemic equilibrium point with control (treatment and TB stigma education campaign) $E^* = \left(S^*, L^*, I_1^*, I_2^*, R^*\right)$ of system (1) using the similar approach as in [16, 22, 26]. Our Lyapunov function is constructed from suitable choice of logarithmic function. The global properties of endemic equilibrium point are studied by starting and proving the following theorem.

Theorem 3: *If* $\Re_e > 1$ *then the unique endemic equilibrium* E^* *of system (1) is globally asymptotically stable.*

Proof: We use similar approach to [20, 21, 23, 25] as it is used to most complicated compartmental epidemiological models to construct the lyapunov function from suitable choice of the following logarithmic function

$$L = \sum_{i=1}^{n} b_i \left(y_i - y_0^* \ln(y_i)\right) \qquad (11c)$$

where, b_i are properly chosen positive constants, y_i is population of compartment i and y_i^* is the equilibrium level. We define the fraction $L : \{(S, L, I_1, I_2, R) \in \Omega : S, L, I_1, I_2, R\} \to R$ by:

$$L(S, L, I_1, I_2, R) = A_1\left(S - S^* \ln(S)\right) + A_2\left(L - L^* \ln(L)\right) + A_3(I_1 - I_1^* \ln(I_1)) + A_4(I_2 - I_2^* \ln(I_2)) + A_5(R - R^* \ln(R)) \qquad (11d)$$

The constants $A_1, A_2, A_3, A_4,$ and A_5 are non-negative in Ω and L is lyapunov function. The function L together with its constants $A_1, A_2, A_3, ..., A_5 > 0$ are chosen in such a way that L is continuous and differentiable in space ∇ and on the interior of Ω, E^* is global minimum of L on Ω, and $L\left(S^*, L^*, I_1^*, I_2^*, R^*\right) = 0.$ The line derivative of lyapunov function L computed along the solution of system (1) is:

$$\frac{dL}{dt} = A_1\left(1 - \frac{S^*}{S}\right)\frac{dS}{dt} + A_2\left(1 - \frac{L^*}{L}\right)\frac{dL}{dt} + A_3\left(1 - \frac{I_1^*}{I_1}\right)\frac{dI_1}{dt} + A_4\left(1 - \frac{I_2^*}{I_{21}}\right)\frac{dI_2}{dt} A_5\left(1 - \frac{R^*}{R}\right)\frac{dR}{dt}. \qquad (11e)$$

At endemic equilibrium point (EEP) we have,

$$\Lambda = \left[\alpha_5 p\lambda + (1-p)\alpha_1\lambda + \mu\right]S^*,$$

$$\mu + \delta\alpha_2 = \frac{1}{L^*}\left[(1-p)\lambda\right]S^*,$$

$$d + \mu + (\phi_1\delta_1 + \tau)_1 + q\eta\alpha_3 = \frac{1}{I_1^*}\left[\alpha_5 pI^*S^* + \delta\alpha_2 L^* + \varepsilon\varphi I_2^* + \phi\alpha_5 I^*R^*\right], \quad (11f)$$

$$\varepsilon\varphi + d + \mu + (1-\varepsilon)\varphi\phi_2 = \frac{1}{I_2^*}\left[q\eta\alpha_3\right]I_1^*,$$

$$\mu = \frac{1}{R^*}\left[(\phi_1\delta_1 + \tau)I_1^* + (1-\varphi)\varepsilon\phi_2 I_2^* - \phi\alpha_4 I^*R^*\right],$$

where $I^* = I_1^* + I_2^*.$

We re-write equation (11e) using (11f) as follows:

$$\begin{aligned}
\frac{dL}{dt} &= A_1\left(1-\frac{S^*}{S}\right)\left\{\left(\alpha_5 p\lambda^* + (1-p)\alpha_1\lambda^* + \mu\right)S^* - \left(\alpha_5 p\lambda^* + (1-p)\lambda^* + \mu\right)S^*\right\},\\
&+ A_2\left(1-\frac{L^*}{L}\right)\left\{(1-p)\alpha_1\lambda^*S^* - \frac{1}{L^*}(1-p)\alpha_1 S^*\right\} +\\
&A_3\left(1-\frac{I_1^*}{I_1}\right)\left\{\delta\alpha_2 L + \varepsilon\varphi I_2 - \frac{1}{I_1^*}\left(\alpha_5 p\lambda^*S^* + \delta\alpha_2 L^* + \varepsilon\varphi I^* + p\varphi\alpha_5 I^*\right)\right\}, \quad (11g)\\
&+ A_4\left(1-\frac{I_2^*}{I_{21}}\right)\left\{q\eta\alpha_3 I_1 - \frac{I_1^*}{I_2^*}\left(q\eta\alpha_3\right)\right\} +\\
&A_5\left(1-\frac{R^*}{R}\right)\left\{(\phi_1\delta_1+\tau)I_1 + (1-\varphi)\varepsilon\phi_2 I_2 - \frac{1}{R^*}\left((\phi_1\delta_1+\tau)I_1^* + (1-\varphi)\varepsilon\phi_2 I_2 - \phi\alpha_4\lambda^*R^*\right)\right\}.
\end{aligned}$$

Simplification of (11g) results to,

$$\frac{dL}{dt} = -A_1\mu\left(\frac{S-S^*}{S}\right)^2 - A_2(1-p)\alpha_1\left(\frac{L-L^*}{L}\right)^2 + M\left(S, L, I_1, I_2, R\right). \quad (11h)$$

The function $M\left(S, L, I_1, I_2, R\right)$ balance the right hand side of (11h). The function $M\left(S, L, I_1, I_2, R\right)$ is non-negative following the approach of [24,25].That is $M \le 0$ for every $S, L, I_1, I_2, R > 0.$ Thus $\frac{dL}{dt} \le 0$ for all $S, L, I_1, I_2, R > 0$ and zero when $S = S^* = 0,\ L = L^* = 0,\ I_1 = I_1^* = 0,\ I_2 = I_2^* = 0,\ R = R^* = 0.$

Therefore the largest compact invariant set in Ω such that $\frac{dL}{dt} = 0$ is the sington $\{E^*\}$ which is Endemic Equilibrium Point of model (1). LaSalle's invariant principle [26] then implies that E^* is globally asymptotically stable in the interior of the region Ω if $\Re_e > 1$ and that complete our proof.

4. Numerical simulations and discussions

In this section numerical simulation of model (1) is carried out in order to illustrate the qualitative results by using available parameter values from existing literature as well as estimated ones. The parameters used during simulation are shown in table 3.

Table 3: Parameter values for model (1)

Symbol	Values (yr^{-1})	Source
Λ	0.03725	[14]
β	0.035	[7]
c	2	[8, 28]
μ	0.013	[14, 15]
d	0.3	[31]
δ	0.02	[14, 15, 20]
α_1	1.25	Estimated
α_2	1.30	Estimated
α_3	1.2	Estimated
α_4	1.4	Estimated
α_5	1.6	Estimated
φ	0.09	Estimated
p	0.05	[9]
ϕ_1	2	[8, 28]
ϕ_2	0.2	Estimated
η	0.4	Assumed
q	0.25	Estimated
ε	0.4	[32]
τ	0.2	[9]
δ_1	0.37	[31]
ϕ	0.21	IDM (2008)

4.1. Numerical Simulation on the variation of Effective Reproduction Number with various involved parameters

In this subsection we performed numerical simulation to see the variation of effective reproduction number $\Re_e$ on different parameters involved with respect to exposure rate.

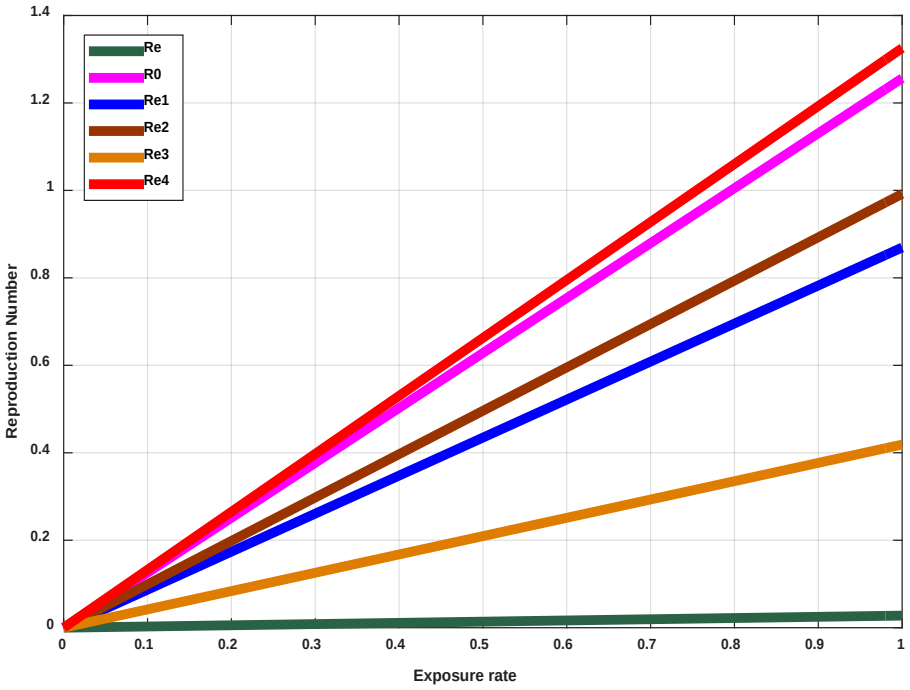

Figure 2: Variation of effective reproduction numbers

The figure above shows the variations of effectives reproduction numbers, where (a) R_e represent effect reproduction number with control strategies (b) R_0 represent basic reproduction number without control strategies (c) R_{e1} represent effective reproduction number with treatment only (d) R_{e2} represent effective reproduction number with education campaign only (e) R_{e3} represent effective reproduction number without stigma (f) R_{e4} represent the effect of stigma on the basic reproduction number.

Figure 2 shows that $\Re_e < \Re_{e3} < \Re_{e1} < \Re_{e2} < \Re_0 < \Re_{e4}$. This means that combination of treatment and TB stigma education campaign is the desirable control strategies in controlling the transmission of TB infection in the community followed by the treatment alone strategy and finally education program to reduce TB stigma. In the absence of TB stigma the results in Figure 2 show that the basic reproduction number $\Re_{e3}$ is very low which means the endemicity of the disease in the community is very low. However, in presence of TB stigma the effective reproduction number $\Re_{e4}$ is very high. This depicts that with TB stigma the transmission increase

in the community. Therefore the results in Figure 2 conclude that in order to fight off TB disease out of the community, there must be properly education program designed purposely to reduce or eliminate TB stigma so that the majority of people in the community volunteer for screening and treatment in order to enable to achieve the millennia goals of eradicating TB out of the community by 2025[7].

4.2. The dynamical behavior of the model system with control strategies

In this subsection we study the dynamical behavior of model (1) in order to see the biological trend of the population of susceptible, exposed, infectious, stigmatized infectious and recovered in the presence of control strategies. See Figure 4 for the numerical simulation results.

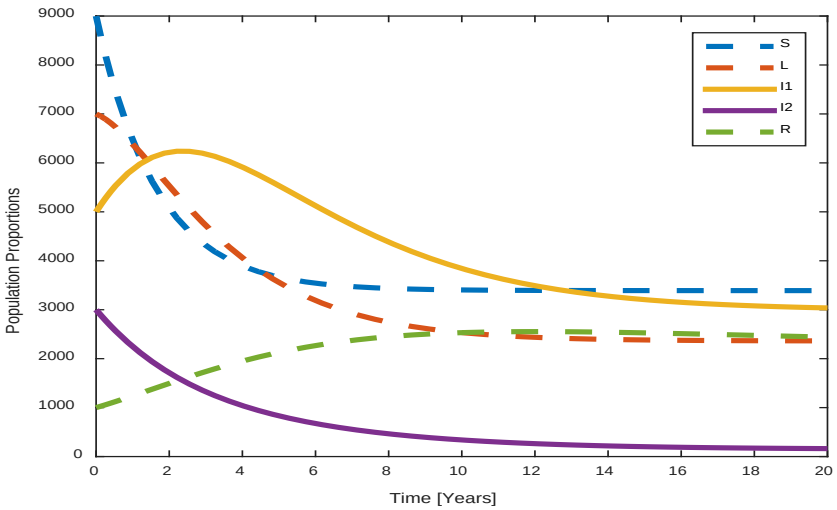

Figure 4: Shows the dynamic of susceptible, latently infected, unstigmatized infectious, stigmatized infectiousand recovered population in presence of control with increasing time.

Figure 4 shows the dynamic behaviour of susceptible, latently infected, unstigmatized infectious, stigmatized infectious and recovered classes. The plot is produced by MATLAB by using the parameter values as shown in Table 3 and their definitions are given in Table 2. Starting with initial values $S(0) = 0.55,\ L(0) = 0.05,$ $I_1(0) = 0.15,\ I_2(0) = 0.12,$ and $R(0) = 0.05.$ In the presence of control strategies, the susceptible population initially decreases to lower levels and later increases to its carrying capacity with time as shown in Figure 2. On the other hand latently infected individuals decrease gradually and later increase to their carrying capacities. Severely infected individuals increase gradually to higher level and later decrease due to treatment and reduction of stigmatized infected population individuals due to education campaign. The recovered population individuals due to treatment of both severely infected and severely stigmatized infected individuals increases to its carrying capacities.

4.3. Impact of Stigma on Prevalence and Incidence of TB Infection

In this subsection we study the impact of introducing stigma to community.

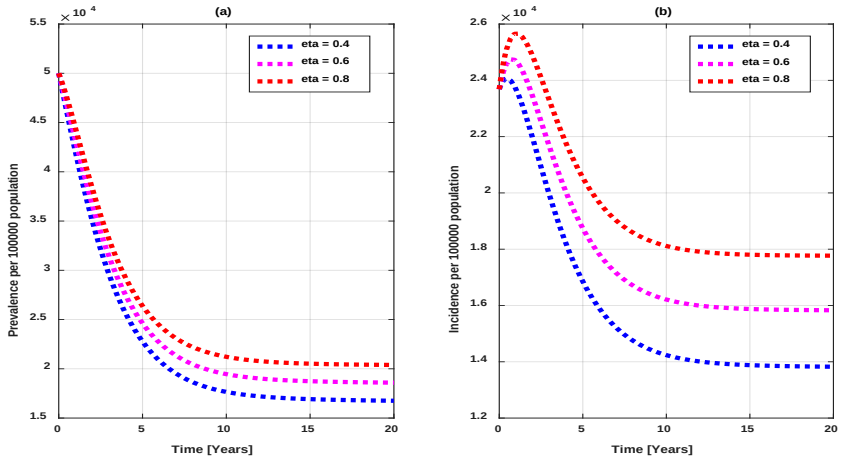

Figure 5: The impact of stigma on disease prevalence and incidence

Figure 5 shows the effects of stigma on prevalence and incidence of the disease, where (a) represent disease prevalence per 100000 population and (b) represent the disease incidence per 100000 population as the rate of stigma vary (eta = 0.4, 0.8, and 1.2).

From Figure 5, the disease prevalence and incidence is high in presence of stigma to the infected population. In particular when stigma increase among the severely infected population the TB infection prevalence and incidence is high in the community as shown in Figure 3. In this case there is need for introducing the intervention strategies that will help to reduce the TB prevalence and incidence by reducing stigma among the infected individuals.

4.4. Impact of Treatment on Prevalence and Incidence of TB Infection

In this subsection, we study the prevalence and incidence of the population when treatment is administered to both unstigmatized infectious population and stigmatized infectious individuals due to education campaign by employing the idea in [16, 21, 30]. In this particular section the treatment rate of both unstigmatized (infectious individuals without stigma) and stigmatized infectious are ϕ_1 and ϕ_2 respectively.

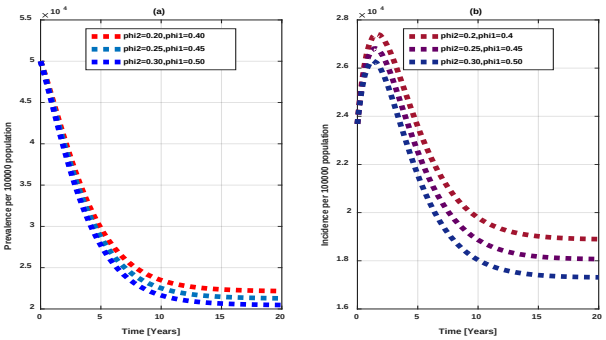

Figure 6: The impact of treatment on disease prevalence and incidence

Figure 6 describe the impact of treatment on the prevalence and incidence of the disease where (a) represent disease prevalence per 100000 population and (b) represent the disease incidence per 100000 populations as treatment vary.

From Figure 6 above, the results show that the prevalence and incidence decreases respectively when the treatment to both infectious individuals increases. We can see clearly from Figure 4 that the prevalence of the disease reduce from 2.25×10^4 to 2.125×10^4 is equivalent to the reduction rate of 12.5%, where the disease incidence reduced from 1.9×10^4 to 1.75×10^4 which is equivalent to the reduction rate of 15%. This is true to say that treatment administration to both unstigmatized infectious and stigmatized infectious is the best strategy to reduce or minimize the prevalence and incidence of the disease respectively.

4.5. Impact of Education Campaign on Prevalence and Incidence of TB Infection

In this subsection, we study the variation of prevalence and incidence of TB disease with different level of education campaign by employing the idea in [16, 17, 21, 30].

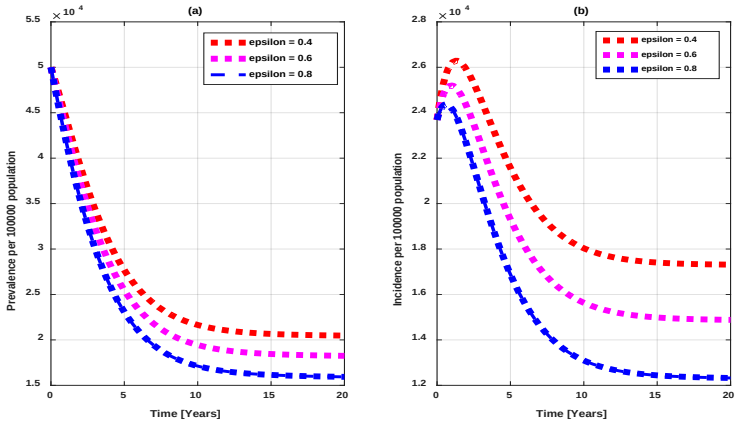

Figure 7: The impact of education campaign on disease prevalence and incidence

Figure 7 shows the impact of education campaign on disease prevalence and incidence where (a) represent disease prevalence per 100000 population and (b) represent the disease incidence per 100000 population as the education campaign level vary (epsilon = 0.2, 0.8 and 1.0).

In Figure 7 above, the prevalence of the disease and incidence decrease slightly as education level increases. This suggest that for proper reduction of prevalence and incidence of the disease rigorous education campaign is needed to reduce the level of stigmatization of infectious individuals in order to control the dynamic of the disease.

4.6. Numerical simulation of model (1) to assess the effect of education campaign and treatment on the prevalence and incidence of TB infection.

In this subsection numerical simulation is done to study the effect of control strategies (treatment and TB stigma education campaign) on the prevalence and incidence of TB infection. Figure 8 below show the numerical results.

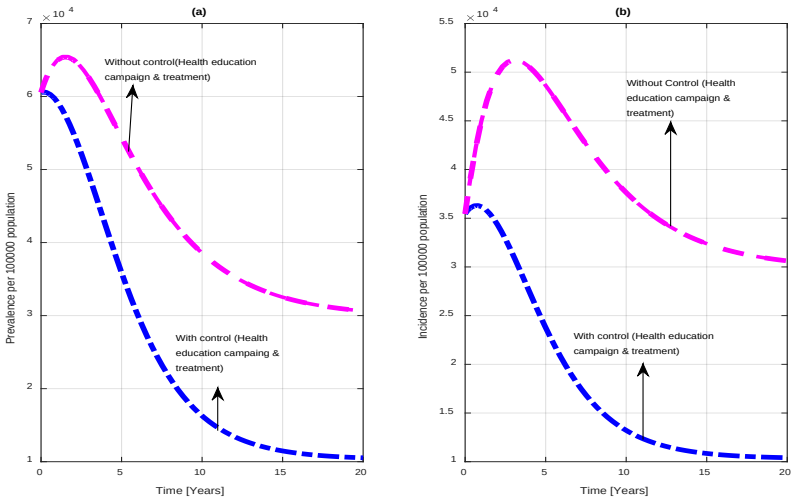

Figure 8: The impact of combined control strategy (health education campaign and treatment) on the prevalence and incidence per 100000 population of the TB infections

Figure 8 show the impact of combined control strategy that is health education campaign and treatment on the prevalence and incidence of TB disease. Figure 7(a) show that there is gradual decline on the prevalence of the disease which can be eliminated out of the community for at least 20 years if property implementation of the strategy is adopted. In Figure 7(b) we clearly see that the effect of combined strategy that is health education campaign and treatment reduce the incidence of the disease to lower levels. That means in order to eliminate the disease from the community the combination of both control strategies (TB stigma education campaign and treatment).

4.7. Numerical simulation showing the effect of Stress and Stigma, treatment and TB stigma education campaign on the dynamics of the disease

Here, numerical simulation is done to understand the effect of stress and stigma (general case), when there is no stress and stigma, stress and stigma without control, stress and stigma with education as the only control strategy, and the effect of stress and stigma with control (treatment and TB stigma education campaign) on the dynamics behavior of TB disease. Figure 9 shows the numerical simulation results.

Figure 5(a), shows the general dynamics of the population. This indicates that the rate of infection is high because many susceptible are infected and there is little recovery. In Figure 5(b) there is large population of recovery and also susceptible population is high. This is because there is high response to treatment for infected individuals when there is no stress and stigma. Figure 5(c) indicates the dynamics of the population when there is no control strategy (education campaign and treatment).

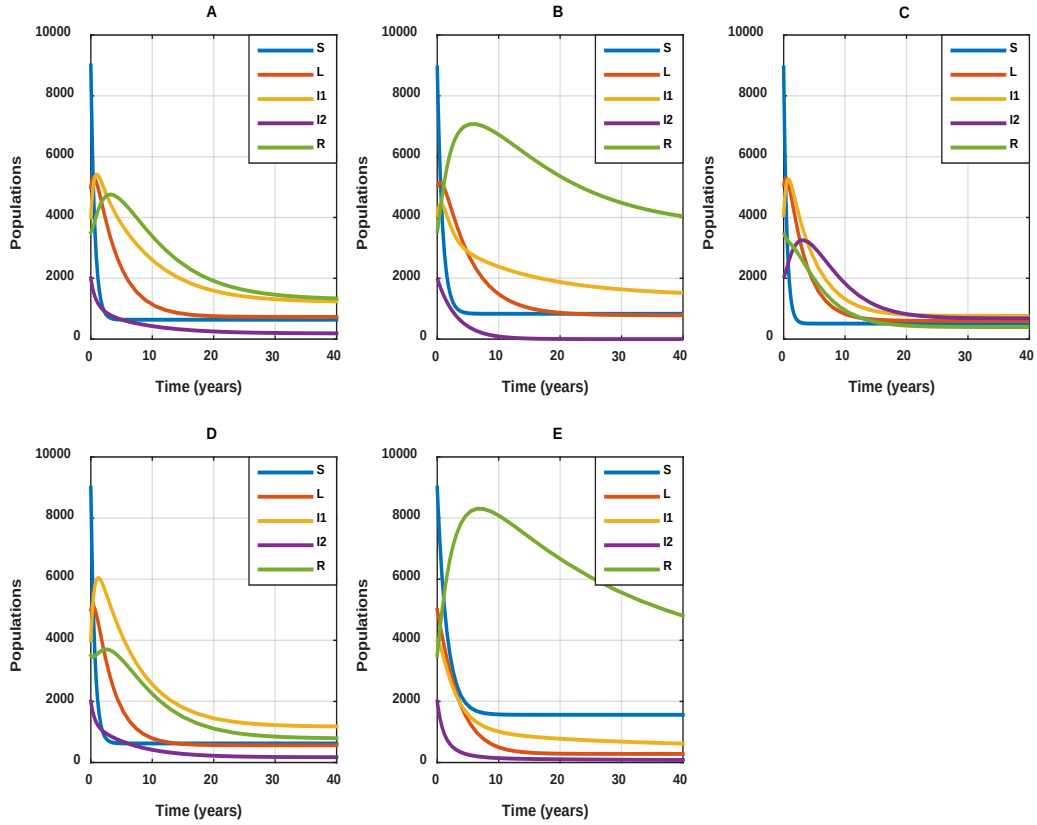

Figure 9: Effect of stress and stigma on the dynamic of the disease, where (a) represents the effect of stress and stigma (General case) (b) No stress and no stigma (c) stress and stigma without control (d) stress and stigma with education campaign as the only control strategy and (e) represent the effect of stress and stigma with control strategies (health education campaign and treatment).

In this case the rate of infection and resistant to treatment is very high that is why the susceptible, latently and recovery population is little as you compare to infectious class.

In Figure 5(d) the administration of education campaign as the only control strategy results to the increase of susceptible, latently and recovery. This may be caused by precaution that will be taken among individuals to avoid new TB cases. Lastly, in Figure 5(e) when health education campaign and treatment are administered we notice a great increase in the number of susceptible and recovery. This is because the level of stress and stigma among the population has been reduced which increased the effect of treatment and hence increase the rate of recovery.

4.8. Limitations of the Study

This study had the following limitations:

- Since the study was compromised by the stigma itself, there was no effective support from the victims to reports their genuine attitudes towards any posted questions.

- Absence of similar studies in the area has made compression of the results difficult.

5. Conclusion

In this paper, a continuous time deterministic model with health education campaign and treatment as control strategies has been formulated to assess the effect on transmission dynamics of Tuberculosis infections. This study point out that stress and stigma are the barrier in controlling TB disease in the community. The disease free equilibrium was obtained and proved using the next generation operator when effective reproduction number $\Re_e < 1$ and unstable otherwise. The numerical simulation results show that in presence of control both severely infected and severely stigmatized infected individuals decrease and stabilize as time increase. Furthermore, the numerical simulation results show that, the combination of both health education campaign and treatment has significant effect toward the eradication of the disease from the community compare to when each strategy is taken separately.

6. Recommendations

Basing on the results of this study we derived the following recommendations:

- More efforts should be made in different working organizations on how to reduce stress and fighting off TB related stigma at working place especially with TB infected individuals.
- More effort should be made to encourage people to voluntarily go for TB test by discouraging stigmatization of people infected by the disease.
- A qualitative study approach can be conducted to have deeper understanding of the factors related to delay. A combination of qualitative and quantitative can be produce better results.
- There is a necessary to conduct further studies to develop models for TB related stigma that allows deeper understanding of this complex cultural construct.
- Programs developed to prevent and control TB disease should address the issue of TB related stigma.
- Communication media including magazine, radios, televisions, e.t.c should be encouraged to be the forefront desk to address the effect of TB related stigma in the control of TB disease.
- Institutions working towards preventions of HIV/AIDS should address the issue of tuberculosis and related stigma.

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