Local Stability Analysis of a Tuberculosis Model incorporating Extensive Drug Resistant Subgroup

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ABSTRACT

This paper proposes a mathematical model for the transmission dynamics of Tuberculosis incorporating extensive drug resistant subgroup. The effective reproduction number R_c was obtained and conditions for local stability of the disease free equilibrium and endemic equilibrium states were established. Numerical simulations confirmed the stability analysis and further revealed that unless proper measures are taken against typical TB, progression to XDR-TB, mortality and morbidity of infected individuals shall continue to rise.

(Keywords: Tuberculosis, extensive drug resistant tuberculosis, effective reproduction number, DFE, XDR, stability)

INTRODUCTION

Tuberculosis (TB) is a chronic airborne disease which is prevalent in developing countries. It is an infectious bacterial disease which normally attacks the respiratory organ (the lungs) and spreads into the bloodstream (Kalu *et al.*, 2012). Tuberculosis strains that are resistant to some of the most efficient drugs used to treat TB, including isoniazid, rifampicin and any one of the three second-line treatment regimens which includes capreomycin, kanamycin or amikacin are generally classified as Extensive drug-resistant *Mycobacterium tuberculosis* (XDR-TB) (Caminero, 2006; Arora, 2008; Kalu *et al.*, 2013 and Caminero *et al.*, 2010).

Nyerere *et al.* (2014); Kalu and Inyama (2012) estimated that up to 10% of infected individuals progress into active TB cases and a great majority of those infected (90%) may live with the disease for a lengthy period without it degenerating into active TB. Despite rigorous efforts to get rid of the disease, tuberculosis is still a key global health issue and continues to be a principal cause of global premature death among infectious diseases worldwide. The initial expectation of the tuberculosis control program began to wane with the evolution of XDR-TB (Lim *et al.*, 2012).

Emergence of XDR-TB is generally attributed to the following factors: incomplete and inadequate treatment, errors in tuberculosis management, such as the use of single antituberculosis drug, failure to identify and address non-compliance to treatment and transmission of drug-resistant strains to new TB cases (Espinal, *et al*., 2001; Young, *et. al*., 2008; Sharma and Mohan, 2013; Eldholm, *et al*., 2014).

It is on record that current treatment regimens for XDR-TB patient are inadequate. Several researchers have revealed in their work that XDR-TB is linked with a much higher death rate and remains contagious for longer periods than other forms of TB. Efforts towards rapid and efficient detection of drug-resistant tuberculosis should therefore be scaled up world-wide, and intensive treatment programs with quality assured drugs should be provided to ensure tuberculosis eradication (Banerjee *et al.*, 2008).

Authors such as Jung, *et al*. (2002), Castillo-Chavez and Feng (1998) and Feng, *et al*. (2002) have used mathematical models to control the transmission dynamics of TB in different parts of the world. In this work, we complement and extend on the aforementioned authors work by incorporating XDR-TB using a non-linear system of ordinary differential equations.

MODEL DEVELOPMENT

A non-linear mathematical model is formulated to study tuberculosis transmission incorporating extensive drug resistant subgroup. Using a compartmental approach, the total population (N) is divided into eight compartments namely; Susceptible individuals (S); Vaccinated individuals (V); Latently infected individuals with typical TB (L); Actively infected individuals with typical TB (I_1); Actively infected individuals with typical TB undergoing treatment (T_1); Actively infected individuals with extensive drug-resistant TB (I_2), Actively infected individuals with extensive drug-resistant TB undergoing treatment (T_2) and Recovered individuals (R). Deaths due to infection occur in I_2, T_1, I_2 and T_2 compartments. Our model has the following variables and parameters:

$S(t)$	Susceptible individuals at time t
$V(t)$	Vaccinated individuals at time t
$L(t)$	Latently infected individuals with typical TB at time t
$I_1(t)$	Actively infected individuals with typical TB at time t
$T_1(t)$	Actively infected individuals with typical TB undergoing treatment at time t
$I_2(t)$	Actively infected individuals with extensive drug-resistant TB at time t
$T_2(t)$	Actively infected individuals with extensive drug-resistant TB undergoing treatment at time t
$R(t)$	Recovered individuals at time t
ω	Waning rate of vaccination
α	Effective contact rate of typical TB
ξ_1	Modification parameter associated with reduced contact rate by actively infected individuals undergoing treatment
ξ_2	Modification parameter associated with reduced contact rate by actively infected individuals with XDR-TB
ξ_3	Modification parameter associated with reduced contact rate by actively infected individuals with XDR-TB undergoing treatment
Λ	Recruitment due to birth
μ	Natural death rate of humans
σ	Progression rate from L to I_1
γ_1	Progression rate from T_1 to R
γ_2	Progression rate from T_2 to R
η	Waning rate of temporal immunity of recovered individuals
ψ_1	Progression rate from T_1 to I_2 due to treatment failure
ψ_2	Progression rate from T_2 to I_2 due to non-compliance with treatment regimen
ρ	Effective immunization rate
δ_1	Mortality rate due to typical TB
δ_2	Mortality rate of TB infected individuals undergoing treatment
δ_3	Mortality rate due to XDR-TB
δ_4	Mortality rate of XDR-TB infected individuals undergoing treatment
τ_1	Treatment rate for individuals with typical TB which is enhanced by DOTS
τ_2	Treatment rate for individuals with extensive drug resistant TB which is enhanced by DOTS

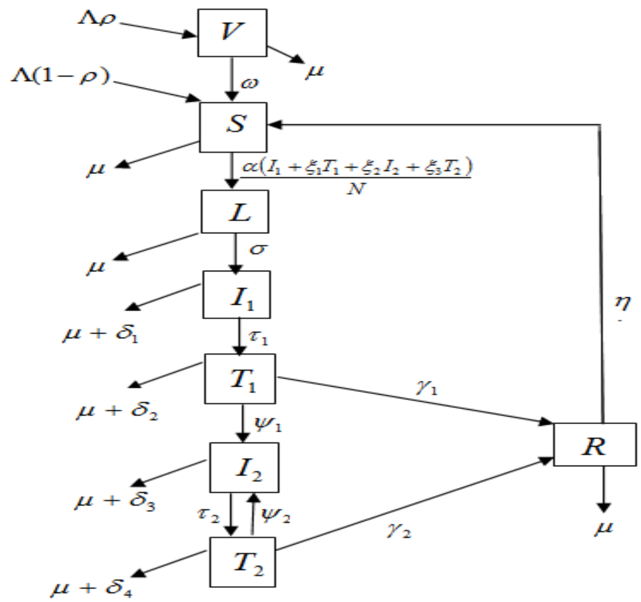

Figure 1: Schematic Representation of TB Transmission Model Incorporating XDR Subgroup.

The mathematical equation of the model is given by system 1:

$$\frac{dS}{dt}=\Lambda(1-\rho)-\frac{\alpha(I_1+\xi_1 T_1+\xi_2 I_2+\xi_3 T_2)S}{N}+\omega V+\eta R-\mu S$$

$$\frac{dV}{dt}=\Lambda\rho-(\omega+\mu)V$$

$$\frac{dL}{dt}=\frac{\alpha(I_1+\xi_1 T_1+\xi_2 I_2+\xi_3 T_2)S}{N}-(\sigma+\mu)L$$

$$\frac{dI_1}{dt}=\sigma L-(\tau_1+\mu+\delta_1)I_1$$

$$\frac{dT_1}{dt}=\tau_1 I_1-(\gamma_1+\psi_1+\mu+\delta_2)T_1$$

$$\frac{dI_2}{dt}=\psi_1 T_1+\psi_2 T_2-(\tau_2+\mu+\delta_3)I_2$$

(1)

$$\frac{dT_2}{dt}=\tau_2 I_2-(\gamma_2+\psi_2+\mu+\delta_4)T_2$$

$$\frac{dR}{dt}=\gamma_1 T_1+\gamma_2 T_2-(\eta+\mu)R$$

where,

$$N=S+V+L+I_1+T_1+I_2+T_2+R.$$

(2)

So that,

$$\frac{dN}{dt}=\Lambda-\mu N-(\delta_1 I_1+\delta_2 T_1+\delta_3 I_2+\delta_4 T_2)$$

(3)

Consider the region,

$$\Omega=(S,V,L,I_1,T_1,I_2,T_2,R)\in\Re_+^8$$

(4)

where Ω is any solution of the system with non-negative initial conditions. It can be shown that the feasible solution set of system (1) enter and remain in the region;

$$\Omega=\left\{(S,V,L,I_1,T_1,I_2,T_2,R)\in\Re_+^8 : N\le\frac{\Lambda}{\mu}\right\}$$

(5)

Let,

$$k_1=\omega+\mu$$

$$k_2=\sigma+\mu$$

$$k_3=\tau_1+\mu+\delta_1$$

$$k_4=\gamma_1+\psi_1+\mu+\delta_2$$

(6)

$$k_5 = \tau_2 + \mu + \delta_3$$

$$k_6 = \gamma_2 + \psi_2 + \mu + \delta_4$$

$$k_7 = \eta + \mu$$

Thus, the system (1) becomes:

$$\frac{dS}{dt} = \Lambda(1-\rho) - \frac{\alpha(I_1 + \xi_1 T_1 + \xi_2 I_2 + \xi_3 T_2)S}{N} + \omega V + \eta R - \mu S$$

$$\frac{dV}{dt} = \Lambda\rho - k_1 V$$

$$\frac{dL}{dt} = \frac{\alpha(I_1 + \xi_1 T_1 + \xi_2 I_2 + \xi_3 T_2)S}{N} - k_2 L$$

$$\frac{dI_1}{dt} = \sigma L - k_3 I_1$$

$$\frac{dT_1}{dt} = \tau_1 I_1 - k_4 T_1 \qquad \textbf{(7)}$$

$$\frac{dI_2}{dt} = \psi_1 T_1 + \psi_2 T_2 - k_5 I_2$$

$$\frac{dT_2}{dt} = \tau_2 I_2 - k_6 T_2$$

$$\frac{dR}{dt} = \gamma_1 T_1 + \gamma_2 T_2 - k_7 R$$

EXISTENCE OF DISEASE FREE EQUILIBRIUM STATE - DFE (E^0)

At equilibrium,

$$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dL}{dt} = \frac{dI_1}{dt} = \frac{dT_1}{dt} = \frac{dI_2}{dt} = \frac{dT_2}{dt} = \frac{dR}{dt} = 0 \qquad \textbf{(8)}$$

let,

$$\begin{pmatrix} S \\ V \\ L \\ I_1 \\ T_1 \\ I_2 \\ T_2 \\ R \end{pmatrix} = \begin{pmatrix} S^0 \\ V^0 \\ L^0 \\ I_1^{\,0} \\ T_1^{\,0} \\ I_2^{\,0} \\ T_2^{\,0} \\ R^0 \end{pmatrix} \quad \text{at DFE} \qquad \textbf{(9)}$$

Substituting (8) and (9) in (7) and solving we obtain the disease free equilibrium state given by:

$$\begin{pmatrix} S^0 \\ V^0 \\ L^0 \\ I_1^{\,0} \\ T_1^{\,0} \\ I_2^{\,0} \\ T_2^{\,0} \\ R^0 \end{pmatrix} = \begin{pmatrix} \dfrac{k_1\Lambda(1-\rho) + \omega\Lambda\rho}{\mu k_1} \\ \dfrac{\Lambda\rho}{k_1} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

(10)

EFFECTIVE REPRODUCTION NUMBER, R_c

By using the method described by Van Den Driessche and Watmough (2002), the effective reproduction number **(** R_c **)** which is the largest eigenvalue (spectral radius ρ) of the next generation matrix, FV^{-1} was derived in Eguda 2016 and is given as:

$$R_c = \frac{(\alpha\sigma k_4 D + \alpha\xi_1\tau_1\sigma D + \alpha\xi_2\psi_1\tau_1\sigma k_6 + \alpha\xi_3\tau_2\psi_1\tau_1\sigma)(k_1\Lambda(1-\rho) + \omega\Lambda\rho)}{N^0 k_2 k_3 k_4 D\mu k_1}$$

(11)

LOCAL STABILITY OF DISEASE- FREE EQUILIBRIUM STATE

The disease free-equilibrium E^0 of the model equations (1) is locally asymptotically stable (LAS) if $R_c < 1$.

Evaluating the Jacobian at the disease free equilibrium to determine the local stability of the system gives:

$$J(E^0) = \begin{pmatrix} -\mu & \omega & 0 & \frac{-\alpha_1 S^0}{N^0} & \frac{-\alpha_2 S^0}{N^0} & \frac{-\alpha_3 S^0}{N^0} & \frac{-\alpha_4 S^0}{N^0} & \eta \\ 0 & -k_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & \frac{\alpha_1 S^0}{N^0} & \frac{\alpha_2 S^0}{N^0} & \frac{\alpha_3 S^0}{N^0} & \frac{\alpha_4 S^0}{N^0} & 0 \\ 0 & 0 & \sigma & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \tau_1 & -k_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \psi_1 & -k_5 & \psi_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_2 & -k_6 & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & 0 & \gamma_2 & -k_7 \end{pmatrix} \quad (12)$$

Computing

$$\left| J(E^0) - \lambda I \right| = 0, \quad (13)$$

for the eigenvalues, we obtain:

$$\lambda_1 = -\mu < 0 \quad (14)$$

$$\lambda_2 = -k_1 = -(\omega + \mu) < 0 \quad (15)$$

$$\lambda_3 = -k_2 = -(\sigma + \mu) < 0 \quad (16)$$

$$\lambda_4 = \frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 \quad (17)$$

For λ_4 to be negative, then;

$$\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 < 0 \quad (18)$$

From (7) at DFE:

$$k_2 k_3 = \frac{\sigma\alpha_1 S^0}{N^0} + \frac{\sigma\left(\alpha_2 T_1^{\,0} + \alpha_3 I_2^{\,0} + \alpha_4 T_2^{\,0}\right) S^0}{N^0 I_1^{\,0}} \quad (19)$$

i.e.,

$$\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 < 0 \quad (20)$$

$$\lambda_5 = \frac{\tau_1 \sigma\alpha_2 S^0}{N^0} + k_4 \left(\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 \right) \quad (21)$$

For λ_5 to be negative, then:

$$\frac{\tau_1 \sigma\alpha_2 S^0}{N^0} + k_4 \left(\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 \right) < 0 \quad (22)$$

From (7) at DFE:

$$k_2 k_3 k_4 = \frac{\tau_1 \sigma\alpha_2 S^0}{N^0} + \frac{\tau_1 \sigma\alpha_1 I_1^{\,0} S^0}{N^0} \frac{k_4}{\tau_1 I_1} + \frac{\tau_1 \sigma\left(\alpha_3 I_2^{\,0} + \alpha_4 T_2^{\,0}\right) S^0}{N^0 T_1^{\,0}} \quad (23)$$

i.e.,

$$\frac{\tau_1 \sigma\alpha_2 S^0}{N^0} + k_4 \left(\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 \right) < 0 \quad (24)$$

Similarly, using the method shown above:

$$\lambda_6 = \frac{\psi_1 \tau_1 \sigma\alpha_3 S^0}{N^0} + k_5 \left(\frac{\tau_1 \sigma\alpha_2 S^0}{N^0} + k_4 \left(\frac{\sigma\alpha_1 S^0}{N^0} - k_2 k_3 \right) \right) < 0 \quad (25)$$

$$\lambda_7 = \left(\frac{\alpha_1 S\sigma}{Nk_2 k_3} + \frac{\alpha_2 S\tau_1 \sigma}{Nk_2 k_3 k_4} + \frac{\alpha_3 S\psi_1 \tau_1 \sigma k_6}{Nk_2 k_3 k_4 D} + \frac{\alpha_4 S\tau_2 \psi_1 \tau_1 \sigma}{Nk_2 k_3 k_4 D} - 1 \right) k_2 k_3 k_4 D \quad (26)$$

$$= \left(R_c - 1\right) k_2 k_3 k_4 D < 0 \tag{27}$$

If $R_c < 1$

$$\lambda_8 = -\left(R_c - 1\right) k_2 k_3 k_4 D \left(\frac{\psi_1 \tau_1 \sigma \alpha_3 S^0}{N^0} + \frac{k_5 \tau_1 \sigma \alpha_2 S^0}{N^0} + \frac{k_5 k_4 \sigma \alpha_1 S^0}{N^0} - k_2 k_3 k_4 k_5 \right) \psi_1 k_7 < 0 \tag{28}$$

If $R_c < 1$

which implies all the eigenvalues have negative real parts if $R_c < 1$:

where

$$D = (k_5 k_6 - \psi_2 \tau_2) \tag{29}$$

Hence, the disease free-equilibrium E^0 of system (1) is locally asymptotically stable (LAS) if $R_c < 1$.

LOCAL STABILITY ANALYSIS OF ENDEMIC EQUILIBRIUM STATE

A bifurcation analysis to illustrate whether the model equations (1) are LAS will be carried out using the Castillo-Chavez and Song (2004) bifurcation theorem as applied in Garba *et al.* (2008) and Abdulrahman *et al.* (2013). The variables are renamed as follows to establish the above;

$$S = x_1, V = x_2, L = x_3, I_1 = x_4,$$
$$T_1 = x_5, I_2 = x_6, T_2 = x_7, R = x_8$$

Applying the vector representation,

$$X = (x_1,\ x_2,\ x_3,\ x_4,\ x_5,\ x_6,\ x_7,\ x_8)^T$$

to the model equations, leads to rewriting (7) in the form given below;

$$\frac{dX}{dt} = F = (f_1,\ f_2,\ f_3,\ f_4,\ f_5,\ f_6,\ f_7,\ f_8)^T$$

Such that:

$$\frac{dx_1}{dt} = f_1 = \Lambda(1-\rho) - \frac{(\alpha x_4 + \alpha\xi_1 x_5 + \alpha\xi_2 x_6 + \alpha\xi_3 x_7)x_1}{N} + \omega x_2 + \eta x_8 - \mu x_1$$

$$\frac{dx_2}{dt} = f_2 = \Lambda\rho - k_1 x_2$$

$$\frac{dx_3}{dt} = f_3 = \frac{(\alpha x_4 + \alpha\xi_1 x_5 + \alpha\xi_2 x_6 + \alpha\xi_3 x_7)x_1}{N} - k_2 x_3 \tag{30}$$

$$\frac{dx_4}{dt} = f_4 = \sigma x_3 - k_3 x_4$$

$$\frac{dx_5}{dt} = f_5 = \tau_1 x_4 - k_4 x_5$$

$$\frac{dx_6}{dt} = f_6 = \psi_1 x_5 + \psi_2 x_7 - k_5 x_6$$

$$\frac{dx_7}{dt} = f_7 = \tau_2 x_6 - k_6 x_7$$

$$\frac{dx_8}{dt} = f_8 = \gamma_1 x_5 + \gamma_2 x_7 - k_7 x_8$$

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8 \le \frac{\Lambda}{\mu} \tag{31}$$

The Jacobian of the system (7) at the DFE is given by:

$$J(E^0)=\begin{pmatrix} -\mu & \omega & 0 & \frac{-\alpha S^0}{N^0} & \frac{-\alpha\xi_1 S^0}{N^0} & \frac{-\alpha\xi_2 S^0}{N^0} & \frac{-\alpha\xi_3 S^0}{N^0} & \eta \\ 0 & -k_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & \frac{\alpha S^0}{N^0} & \frac{\alpha\xi_1 S^0}{N^0} & \frac{\alpha\xi_2 S^0}{N^0} & \frac{\alpha\xi_3 S^0}{N^0} & 0 \\ 0 & 0 & \sigma & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \tau_1 & -k_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \psi_1 & -k_5 & \psi_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_2 & -k_6 & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & 0 & \gamma_2 & -k_7 \end{pmatrix} \tag{32}$$

Suppose that $\phi=\alpha$ is chosen as the bifurcation parameter, it will be shown whether the model system exhibits a backward or forward bifurcation at $R_c=1$ (Gumel and Song, 2008). Let V and W correspond to the left and right eigenvectors such that $VJ(E_0)=0$ and $J(E_0)W=0$.

$$VJ(E^0)=(v_1,v_2,v_3,v_4,v_5,v_6,v_7\ v_8)\begin{pmatrix} -\mu & \omega & 0 & \frac{-\alpha S^0}{N^0} & \frac{-\alpha\xi_1 S^0}{N^0} & \frac{-\alpha\xi_2 S^0}{N^0} & \frac{-\alpha\xi_3 S^0}{N^0} & \eta \\ 0 & -k_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & \frac{\alpha S^0}{N^0} & \frac{\alpha\xi_1 S^0}{N^0} & \frac{\alpha\xi_2 S^0}{N^0} & \frac{\alpha\xi_3 S^0}{N^0} & 0 \\ 0 & 0 & \sigma & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \tau_1 & -k_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \psi_1 & -k_5 & \psi_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_2 & -k_6 & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & 0 & \gamma_2 & -k_7 \end{pmatrix}=\begin{pmatrix}0\\0\\0\\0\\0\\0\\0\\0\end{pmatrix} \tag{33}$$

Solving the above gives:

$$v_1=v_2=v_8=0$$

$$v_3=\frac{\sigma N\tau_1\tau_2\psi_1 v_7}{Nk_2k_3k_4k_5-\alpha S\sigma k_4k_5-\alpha\xi_1 S\sigma\tau_1k_5-\alpha\xi_2 S\sigma\tau_1\psi_1}$$

$$v_4=\frac{Nk_2\tau_1\tau_2\psi_1 v_7}{Nk_2k_3k_4k_5-\alpha S\sigma k_4k_5-\alpha\xi_1 S\sigma\tau_1k_5-\alpha\xi_2 S\sigma\tau_1\psi_1}$$

$$v_5=\frac{\psi_1\left(Nk_2k_3-\alpha_1 S\sigma\right)\tau_2 v_7}{Nk_2k_3k_4k_5-\alpha S\sigma k_4k_5-\alpha\xi_1 S\sigma\tau_1k_5-\alpha\xi_2 S\sigma\tau_1\psi_1}$$

$$v_6=\frac{\left(Nk_2k_3k_4-\alpha_1 S\sigma k_4-\alpha_2 S\sigma\tau_1\right)\tau_2 v_7}{Nk_2k_3k_4k_5-\alpha S\sigma k_4k_5-\alpha\xi_1 S\sigma\tau_1k_5-\alpha\xi_2 S\sigma\tau_1\psi_1}$$

v_7 can take any value

Similarly,

$$J(E^0)W=\begin{pmatrix} -\mu & \omega & 0 & \frac{-\alpha S^0}{N^0} & \frac{-\alpha\xi_1 S^0}{N^0} & \frac{-\alpha\xi_2 S^0}{N^0} & \frac{-\alpha\xi_3 S^0}{N^0} & \eta \\ 0 & -k_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_2 & \frac{\alpha S^0}{N^0} & \frac{\alpha\xi_1 S^0}{N^0} & \frac{\alpha\xi_2 S^0}{N^0} & \frac{\alpha\xi_3 S^0}{N^0} & 0 \\ 0 & 0 & \sigma & -k_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \tau_1 & -k_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \psi_1 & -k_5 & \psi_2 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau_2 & -k_6 & 0 \\ 0 & 0 & 0 & 0 & \gamma_1 & 0 & \gamma_2 & -k_7 \end{pmatrix}\begin{pmatrix}w_1\\w_2\\w_3\\w_4\\w_5\\w_6\\w_7\\w_8\end{pmatrix}=\begin{pmatrix}0\\0\\0\\0\\0\\0\\0\\0\end{pmatrix} \tag{34}$$

Solving yields:

$$w_1=\left(\frac{\eta N^0\tau_1 H-\alpha SDk_4k_7-\alpha\xi_1 S\tau_1 Dk_7-\alpha\xi_2 S\tau_1k_6k_7\psi_1-\alpha\xi_3 S\tau_1\tau_2\psi_1k_7}{\mu N^0\tau_1 H}\right)w_8$$

$$w_2 = 0, \quad w_3 = \frac{k_3 k_4 k_7 D w_8}{\sigma \tau_1 H}, \quad w_4 = \frac{k_4 k_7 D w_8}{\tau_1 H}, \quad w_5 = \frac{k_7 D w_8}{H}$$

$$w_6 = \frac{\psi_1 k_6 k_7 w_8}{H}, \quad w_7 = \frac{\psi_1 \tau_2 k_7 w_8}{H}, \quad w_8 > 0$$

Where,

$$H = \left(\gamma_1 k_5 k_6 + \gamma_2 \psi_1 \tau_2 - \gamma_1 \tau_2 \psi_2\right) \qquad \textbf{(35)}$$

Applying the Castillo-Chavez and Song (2004) stability theorem to get the conditions for the existence of forward or backward bifurcation by verifying the signs of a and b gives:

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$$

$$a = \frac{2 v_3 w_1}{N^0}\left(w_4 \alpha + w_5 \alpha \xi_1 + w_6 \alpha \xi_2 + w_7 \alpha \xi_3\right) \qquad \textbf{(36)}$$

$$a = \frac{\begin{bmatrix} 2\sigma \tau_1 \tau_2 \psi_1 v_7 w_8 \left(\alpha D k_4 + \alpha \xi_1 D \tau_1 + \alpha \xi_2 \psi_1 k_6 \tau_1 + \alpha \xi_3 \psi_1 \tau_1 \tau_2\right) k_7 w_8 \\ \times \left(\eta N^0 \tau_1 H - \alpha S D k_4 k_7 - \alpha \xi_1 S \tau_1 D k_7 - \alpha \xi_2 S \tau_1 k_6 k_7 \psi_1 - \alpha \xi_3 S \tau_1 \tau_2 \psi_1 k_7\right) \end{bmatrix}}{H N^0 \tau_1 \mu \tau_1 H \left(N k_2 k_3 k_4 k_5 - \alpha S \sigma k_4 k_5 - \alpha \xi_1 S \sigma \tau_1 k_5 - \alpha \xi_2 S \sigma \tau_1 \psi_1\right)} \qquad \textbf{(37)}$$

$$H = \left(\gamma_1 k_5 k_6 + \gamma_2 \psi_1 \tau_2 - \gamma_1 \tau_2 \psi_2\right) > 0 \qquad \textbf{(38)}$$

From (25),

$$N k_2 k_3 k_4 k_5 - \alpha S \sigma k_4 k_5 - \alpha \xi_1 S \sigma \tau_1 k_5 - \alpha \xi_2 S \sigma \tau_1 \psi_1 > 0 \qquad \textbf{(39)}$$

Therefore, from (37), $a > 0$

Whenever,

$$\alpha < \frac{\eta N^0 \tau_1 H}{S^0 D k_4 k_7 + \xi_1 S^0 \tau_1 D k_7 + \xi_2 S^0 \tau_1 k_6 k_7 \psi_1 + \xi_3 S^0 \tau_1 \tau_2 \psi_1 k_7} \qquad \textbf{(40)}$$

Similarly,

$$b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0)$$

Let $\alpha = \phi$ be chosen as the bifurcation parameter
for $k = 1, 2, 8$ $v_1 = v_2 = v_8 = 0$

Since $x_4 = x_5 = x_6 = x_7 = 0$ at DFE

$$b = \frac{x_1 v_3}{N^0}\left(w_4 + \xi_1 w_5 + \xi_2 w_6 + \xi_3 w_7\right) \qquad \textbf{(41)}$$

which becomes:

$$b = \frac{x_1 \sigma \tau_1 \tau_2 \psi_1 v_7 \left(k_4 D + \tau_1 \xi_1 D + \tau_1 \psi_1 \xi_2 k_6 + \tau_1 \psi_1 \tau_2 \xi_3\right) k_7 w_8}{\left(N k_2 k_3 k_4 k_5 - \alpha S \sigma k_4 k_5 - \alpha \xi_1 S \sigma \tau_1 k_5 - \alpha \xi_2 S \sigma \tau_1 \psi_1\right)\left(\gamma_1 k_5 k_6 + \gamma_2 \psi_1 \tau_2 - \gamma_1 \tau_2 \psi_2\right)} \qquad \textbf{(42)}$$

From (38) and (39), we have:

$b > 0.$
If $R_c > 1$,

(1) From (40), the endemic equilibrium state is locally asymptotically stable for R_c close to 1, if,

$$\alpha < \frac{\eta N^0 \tau_1 H}{S^0 D k_4 k_7 + \xi_1 S^0 \tau_1 D k_7 + \xi_2 S^0 \tau_1 k_6 k_7 \psi_1 + \xi_3 S^0 \tau_1 \tau_2 \psi_1 k_7} \qquad \textbf{(43)}$$

(2) A backward bifurcation occurs at $\phi = 0$ and the endemic equilibrium state is unstable if,

$$\alpha > \frac{\eta N^0 \tau_1 H}{S^0 D k_4 k_7 + \xi_1 S^0 \tau_1 D k_7 + \xi_2 S^0 \tau_1 k_6 k_7 \psi_1 + \xi_3 S^0 \tau_1 \tau_2 \psi_1 k_7} \qquad \textbf{(44)}$$

The inequality (44) is an upper bound for stability. If the effective contact rate goes beyond this bound, the endemic equilibrium state becomes unstable and a state called backward bifurcation occurs.

RESULTS AND DISCUSSION

Numerical simulations are presented here using appropriate set of parameter values to illustrate the dynamics of the model for various values of the effective reproduction number in order to confirm the local stability of the disease free equilibrium state and establish a criterion for the local stability of the endemic equilibrium state whenever R_c is near one. Parameter values are estimated based on tuberculosis data studies shown in table 1 below as in Eguda *et al.* (2016) and are used for the simulations.

Table 1: Baseline Values for Population-Independent Parameters of the Model (yr^{-1}).

No	Parameter	Value	S/No	Parameter	Value
1	α	0.0000621	10	ψ_2	0.06
2	ξ_1	0.826	11	δ_1	0.00292
3	ξ_2	0.296	12	δ_2	0.00032
4	ξ_3	0.050	13	δ_3	0.00144
5	ω	0.067	14	δ_4	0.0005
6	σ	0.5	15	η	0.4
7	γ_1	2	16	ρ, τ_1, τ_2	(0-1)
8	γ_2	0.5	17	μ	0.0189
9	ψ_1	0.226	18	Λ	3,348,245

NUMERICAL SIMULATIONS

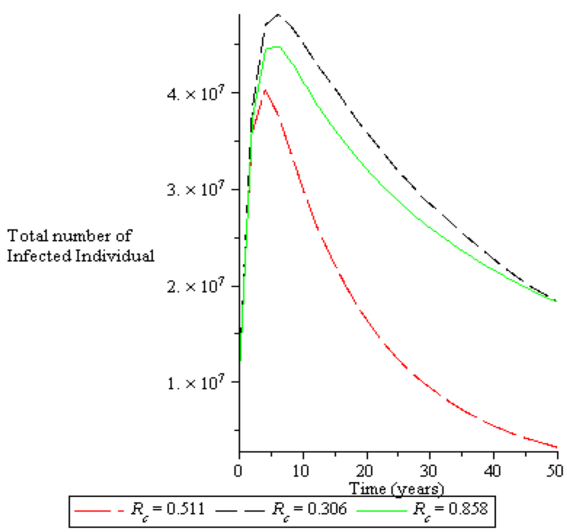

Figure 2: Total Number of Infected Individuals with Three Different Effective Reproduction Numbers which are less than Unity.

(Control parameters used are $\tau_1 = \tau_2 = \rho = 0.1$ with $\alpha = 0.0621$ which gives $R_c = 0.511$; $\tau_1 = \tau_2 = \rho = 0.01$ with $\alpha = 0.01$ which gives $R_c = 0.306$; $\tau_1 = \tau_2 = \rho = 0.05$ with $\alpha = 0.0621$ which gives $R_c = 0.858$).

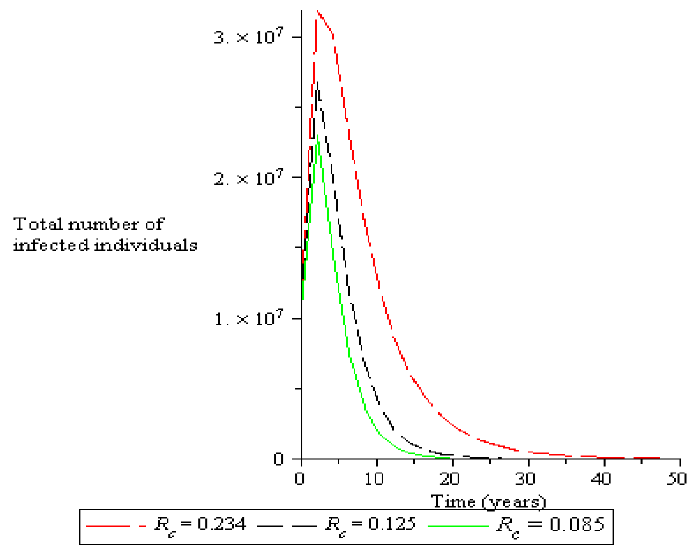

Figure 3: Total Number of Infected Individuals with Three Different Control Levels.

Control parameters used are $\tau_1 = \tau_2 = \rho = 0.25$ with $\alpha = 0.0621$ which gives $R_c = 0.234$; $\tau_1 = \tau_2 = \rho = 0.25$ with $\alpha = 0.0621$ which gives $R_c = 0.125$; $\tau_1 = \tau_2 = \rho = 0.75$ with $\alpha = 0.0621$ which gives $R_c = 0.085$.

CONCLUSION

The result shows local stability of the disease free equilibrium, which hold if $R_c < 1$. Figure 2 shows the local stability of the disease free equilibrium state. It shows for different values of the effective reproduction number, the total number of infected individuals decreases while Figure 3 shows that the solution profiles converge to the disease free equilibrium which confirms the result obtained in our stability analysis. Hence it is possible to control the disease irrespective of the population of infected if proper measures are taken towards reducing progression from typical TB to extensive drug resistant TB.

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