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Stability Analysis of a Deterministic Compartmental Model of Tuberculosis with Effect of HIV/AIDS on the Progression from Latent Class to Infectious Class

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Abstract

In 2015, there were an estimated 10.4 million new (incident) Tuberculosis cases worldwide, of which 5.9 million (56%) were among men, 3.5 million (34%) among women and 1.0 million (10%) among children. People living with HIV accounted for 1.2 million (11%) of all new TB cases. Six countries accounted for 60% of the new cases: India, Indonesia, China, Nigeria, Pakistan and South Africa [3]. In this study we present a deterministic compartmental mathematical

model for the dynamics of tuberculosis and incorporate parameters for slow and fast progression from latently infected tuberculosis to infectious tuberculosis using a modified SIS model to show the effect of HIV/AIDS on the spread of Tuberculosis. The disease free and endemic equilibrium states were established. The disease free equilibrium state was analyzed for stability using a modified version of Bellman and Cooke theorem [1].

1   Introduction

With the increasing reported cases of Tuberculosis in Nigeria which is further compounded by high National HIV prevalence of 3.4%, Tuberculosis was declared an emergency in Nigeria and the Stop TB strategy for the control of TB in Nigeria was adopted to reduce the prevalence of Tuberculosis to a level at which the disease will no longer constitute public health problems in the country with the goal to reduce, significantly, the burden of TB by 2015 in line with the Millennium Development Goals (MDGs) and the STOP TB Partnership targets [4].

The Sustainable Development Goals (SDGs) for 2030 were adopted by the United Nations in 2015. One of the targets is to end the global TB epidemic. The WHO End TB Strategy, approved by the World Health Assembly in 2014, calls for a 90% reduction in TB deaths and an 80% reduction in the TB incidence rate by 2030, compared with 2015 [3].

Of all people living with HIV globally, 9% of them live in Nigeria, which together with South Africa and Uganda, account for almost half of all annual new HIV infections in sub-Saharan Africa. This is despite achieving a 35% reduction in new infections between 2005 and 2013. Approximately 210,000 people died from AIDS-related illnesses in Nigeria in 2013, which is 14% of the global total. Since 2005, there has been no reduction in the number of annual deaths, indicative of the fact that only 20% of people living with HIV in Nigeria are accessing antiretroviral treatment (ART) [8].

Efforts have been made in the past to use Mathematical models to predict the effect of HIV/AIDS on Tuberculosis. Okyere [5] proposed a deterministic compartmental model of HIV and TB but this model did not take into

account that latently infected individual can recover without progressing to infectious class. He also stated that successfully treated infectious individuals move back to slow rate Latent class. This is not only realistic but happens when reinfection occurs; otherwise, they move into recovered class.

Yusuf [7] also proposed a deterministic compartmental model but ignored the different rates of progression from latent to infectious class; however, this precludes the speedy progression of TB caused by HIV infections.

Hughes et al [2] established that progression to active TB is rapid if it occurs within 5 years after infection. In the same paper, they stated that 14% of HIV negative people or early HIV positive people develop active TB within these five years after which the progression is slow which is 0.001/year. Also 67% of people who are in their late stage of HIV develop TB within 5 years after which the progression is slow, 0.1/year.

Based on the above we present a new deterministic compartmental mathematical model for the dynamics of tuberculosis and incorporate parameters for slow and fast progression from latently infected tuberculosis to infectious tuberculosis using a modified SIS model, which is different from the approaches used in some of the papers cited above.

2 The model equations

The model equations for the dynamical system is given by the following system of ordinary differential equations:

$$\frac{dS}{dt} = \rho - \mu S - \beta IS + \varepsilon L_S + \psi L_F + \phi I \tag{2.1}$$

$$\frac{dL_S}{dt} = \theta \beta IS - (\mu + \gamma + \varepsilon) L_S \tag{2.2}$$

$$\frac{dL_F}{dt} = (1 - \theta)\beta IS + \gamma L_S - (\mu + \tau + \psi) L_F \tag{2.3}$$

$$\frac{dI}{dt} = \tau L_F - (\mu + \delta + \phi) I \tag{2.4}$$

The model parameters and variables are given below with their respective descriptions.

$S(t)$: The number of Susceptible individuals at time t.
$L_S(t)$: The number of Latently infected individuals with slow progression rate to infectious class at time t.
$L_F(t)$: The number of Latently infected individuals with fast progression rate to infectious class at time t.
$I(t)$: The number of Infectious individuals at time t.
ρ: Recruitment rate.
μ : Natural death rate.
β: Tuberculosis contraction rate..
θ : proportion of infection instantaneous incidence rate with slow progression rate to infectious TB.
γ : Movement rate from Latent class with slow progression rate to Latent class with fast progression rate.
τ : Movement rate from Latent class with fast progression rate to infectious class.
δ: Tuberculosis induced death rate
ε: Recovery rate of L_S
ψ: Recovery rate of L_F
ϕ: Recovery rate of I
In this study we assumed that there is homogeneous mixing of the population where all people are equally likely to be infected by infectious individuals in case of contact. We also assumed for simplicity that each compartment has equal natural death rateμ. It is only at the late stage of HIV/AIDS that the immune system become weak and influences the progression from Latent class to Infectious Class. Hence early HIV-positive individuals behave in the same way as HIV-negative patients (Hughes et al [2]).

It is important to note that in this model, we also assumed that successfully cured individuals from Latent and infectious class becomes susceptible immediately after their treatments and could be re-infected again whenever they are re-exposed to TB infection irrespective of their Tuberculosis infection history. Realistically this group may enjoy some temporary immunity to tuberculosis infection and whenever they are re infected, they may require more intensive treatment as a result of some multi drug resistance that must

have been built over time.

2.1   Equilibrium state of the model

We solved the model equations simultaneously and obtained the following equilibrium states.
$(w, x, y, z) = (\frac{\rho}{\mu},0,0,0)$ as the disease free equilibrium state which is the state of complete eradication of Tuberculosis from Nigeria and

$$w = \frac{(\mu + \tau + \psi)(\mu + \delta + \phi)(\mu + \gamma + \varepsilon)}{\tau[(1 - \theta)\beta(\mu + \gamma + \varepsilon) + \gamma\theta\beta]},$$

$$x = \frac{(\mu + \tau + \psi)(\mu + \delta + \phi)\theta\beta z}{\tau[(1 - \theta)\beta(\mu + \gamma + \varepsilon) + \gamma\theta\beta]}, y = \frac{Z(\mu + \delta + \phi)}{\tau}$$

$$z = \frac{\rho\tau[(1 - \theta)\beta(\mu + \gamma + \varepsilon) + \gamma\theta\beta] - \mu(\mu + \tau + \psi)(\mu + \delta + \phi)(\mu + \gamma + \varepsilon)}{(\mu + \delta)\tau[(1 - \theta)\beta(\mu + \gamma + \varepsilon) + \gamma\theta\beta] + \mu(\mu + \delta + \phi)\{(\mu + \tau + \psi)\theta\beta + [(1 - \theta)\beta(\mu + \gamma + \varepsilon) + \gamma\theta\beta]\}}$$

as the endemic equilibrium state.

3   Stability analysis of the equilibrium states

Having established the disease free and the endemic equilibrium states, we now investigate the stability of the equilibrium states. To obtain this, we examine the behaviour of the model population near the equilibrium states.

3.1   The characteristic equation

The Jacobian matrix of the system equations is given by

$$J = \begin{pmatrix} -(\mu + \beta z) & \varepsilon & \psi & \phi - \beta w \\ \theta\beta z & -(\mu + \gamma + \varepsilon) & 0 & \theta\beta w \\ (1 - \theta)\beta z & \gamma & -(\mu + \tau + \psi) & (1 - \theta)\beta w \\ 0 & 0 & \tau & -(\mu + \delta + \phi) \end{pmatrix}$$

The characteristic equation is obtained from the Jacobian determinant with the eigenvalues λ:

$$-(\mu + \beta z + \lambda)\{-(\mu + \gamma + \varepsilon + \lambda)[(\mu + \tau + \psi + \lambda)(\mu + \delta + \phi + \lambda) - (1 - \theta)\beta\tau w] + \theta\beta w\gamma\tau\}$$
$$-\varepsilon\{\theta\beta z(\mu + \tau + \psi + \lambda)(\mu + \delta + \phi + \lambda)\}$$
$$+\psi\{-(\mu + \delta + \phi + \lambda)[\theta\beta z\gamma + (\mu + \gamma + \varepsilon + \lambda)(1 - \theta)\beta z]\}$$
$$-(\phi - \beta w)\{\theta\beta z\gamma\tau + (\mu + \delta + \phi + \lambda)(1 - \theta)\beta\tau z\} = 0$$

$$(3.5)$$

3.2　Stability analysis of the disease free equilibrium state

At the disease free equilibrium state $(w,x,y,z) = (\frac{\rho}{\mu}, 0, 0, 0)$. Hence the characteristic equation takes the form

$$-(\mu + \lambda)\{-(\mu + \gamma + \varepsilon + \lambda)[(\mu + \tau + \psi + \lambda)(\mu + \delta + \varphi + \lambda) -$$
$$(1 - \theta)\beta\tau(\frac{\rho}{\mu})] + \theta\beta(\frac{\rho}{\mu})\gamma\tau\} = 0 \qquad (3.6)$$

$$\Rightarrow -(\mu + \lambda) = 0 \qquad (3.7)$$

or

$$\{-(\mu + \gamma + \varepsilon + \lambda)[(\mu + \tau + \psi + \lambda)(\mu + \delta + \phi + \lambda) - (1 - \theta)\beta\tau(\frac{\rho}{\mu})] + \theta\beta(\frac{\rho}{\mu})\gamma\tau\} = 0 \qquad (3.8)$$

Consequently, $\lambda = -\mu$.

4　Nature of Eigenvalues

To establish the nature of eigenvalues in (3.4), we now apply:

Bellman and Cooke theorem [1]:
Let $H(z) = P(z, e^z)$, where $p(z, w)$ is a polynomial with principal term.
Suppose $H(iy), y\varepsilon\mathbf{R}$, is separated into its real and imaginary parts,
$H(z) = F(y) + iG(y)$.
If all zeros of $H(z)$ have negative real parts, then the zeros of $F(y)$ and $G(y)$ are real, simple and alternating and

$G'(0)F(0) - G(0)F'(0) > 0$ for all $y \in \mathbf{R}$.

Conversely, all zeros of $H(z)$ will be in the left-half plane provided that either of the following conditions is satisfied:

(i) All the zeros of $F(y)$ and $G(y)$ are real, simple, and alternating.

(ii) All the zeros of $F(y)$ are real.

(iii) All the zeros of $G(y)$ are real.

Let $H(\lambda) = -(\mu + \gamma + \varepsilon + \lambda)[(\mu + \tau + \psi + \lambda)(\mu + \delta + \phi + \lambda) - (1 - \theta)\beta\tau(\frac{\rho}{\mu})] + \theta\beta(\frac{\rho}{\mu})\gamma\tau$

$$H(\lambda) = -\lambda^3 - \lambda^2[(\mu + \delta + \gamma) + (\mu + \eta + \psi) + (\mu + \pi + \varepsilon)]$$
$$-\lambda[(\mu + \eta + \psi)(\mu + \delta + \gamma) + (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) + (\mu + \eta + \psi)(\mu + \pi + \varepsilon)$$
$$-(1 - \theta)\beta\eta(\frac{\rho}{\mu})] - [(\mu + \eta + \psi)(\mu + \delta + \gamma)(\mu + \pi + \varepsilon) - (\mu + \pi + \varepsilon)(1 - \theta)\beta\eta(\frac{\rho}{\mu})$$
$$-\theta\beta(\frac{\rho}{\mu})\pi\eta]$$

We now set $\lambda = iw$ and then apply the result of Bellman and Cooke, as applied by Sirajo [10], to analyze the disease free equilibrium state for stability or otherwise.

$$H(\lambda) = -(iw)^3 - (iw)^2[(\mu + \delta + \gamma) + (\mu + \eta + \psi) + (\mu + \pi + \varepsilon)]$$
$$-(iw)[(\mu + \eta + \psi)(\mu + \delta + \gamma) + (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) + (\mu + \eta + \psi)(\mu + \pi + \varepsilon) - (1 - \theta)\beta\eta(\frac{\rho}{\mu})]$$
$$-[(\mu + \eta + \psi)(\mu + \delta + \gamma)(\mu + \pi + \varepsilon) - (\mu + \pi + \varepsilon)(1 - \theta)\beta\eta(\frac{\rho}{\mu}) - \theta\beta(\frac{\rho}{\mu})\pi\eta]$$

$$H(\lambda) = iw^3 + w^2[(\mu + \delta + \gamma) + (\mu + \eta + \psi) + (\mu + \pi + \varepsilon)]$$
$$-iw[(\mu + \eta + \psi)(\mu + \delta + \gamma) + (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) + (\mu + \eta + \psi)(\mu + \pi + \varepsilon) - (1 - \theta)\beta\eta(\frac{\rho}{\mu})]$$
$$-[(\mu + \eta + \psi)(\mu + \delta + \gamma)(\mu + \pi + \varepsilon) - (\mu + \pi + \varepsilon)(1 - \theta)\beta\eta(\frac{\rho}{\mu}) - \theta\beta(\frac{\rho}{\mu})\pi\eta]$$

Resolving into real and imaginary parts we have,

$$H(iw) = F(w) + iG(w)$$

$F(w)$ *and* $G(w)$ are given respectively by

$$F(w) = w^2[(\mu + \delta + \gamma) + (\mu + \eta + \psi) + (\mu + \pi + \varepsilon)] - [(\mu + \eta + \psi)(\mu + \delta + \gamma)(\mu + \pi + \varepsilon)$$
$$-(\mu + \pi + \varepsilon)(1 - \theta)\beta\eta(\frac{\rho}{\mu}) - \theta\beta(\frac{\rho}{\mu})\pi\eta]$$

$$G(w) = w^3 - w[(\mu + \eta + \psi)(\mu + \delta + \gamma) + (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) + (\mu + \eta + \psi)(\mu + \pi + \varepsilon)$$
$$-(1 - \theta)\beta\eta(\frac{\rho}{\mu})]$$

Differentiating with respect to w, we have
$$F'(w) = 2w[(\mu + \delta + \gamma) + (\mu + \eta + \psi) + (\mu + \pi + \varepsilon)]$$

$$G'(w) = 3w^2 - [(\mu + \eta + \psi)(\mu + \delta + \gamma) + (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) + (\mu + \eta + \psi)(\mu + \pi + \varepsilon)$$
$$-(1 - \theta)\beta\eta(\tfrac{\rho}{\mu})]$$

Setting $w = 0$, we have
$$F(0) = (\mu + \pi + \varepsilon)(1 - \theta)\beta\eta(\frac{\rho}{\mu}) + \theta\beta(\frac{\rho}{\mu})\pi\eta - (\mu + \eta + \psi)(\mu + \delta + \gamma)(\mu + \pi + \varepsilon)$$

$$G(0) = 0$$

$$F'(0) = 0$$

$$G'(0) = (1 - \theta)\beta\eta(\frac{\rho}{\mu}) - (\mu + \eta + \psi)(\mu + \delta + \gamma) - (\mu + \delta + \gamma)(\mu + \pi + \varepsilon) - (\mu + \eta + \psi)(\mu + \pi + \varepsilon)$$

The condition for Re$\lambda < 0$ according to the result of Bellman and Cooke [1] is given by
$$F(0)G'(0) + F'(0)G(0) > 0 \qquad (4.9)$$

Since $G(0) = 0$, $F(0)G'(0) > 0$
Let $J = F(0)G'(0)$. We must have $J > 0$.
Using hypothetical values for parameters of J and using the mathematical software Maple to evaluate J, the results are presented in the following table:

Table 4.1

ρ	β	θ	ε	ψ	π	η	γ	δ	μ	J	Remark
0.25	0.1	0.5	1.0	1.0	0.1	0.1	0.6	0.15	0.1	4.187873	Stable
0.25	0.2	0.5	0.9	0.9	0.2	0.2	0.6	0.15	0.1	3.95922	Stable
0.25	0.3	0.5	0.8	0.8	0.3	0.3	0.6	0.15	0.1	3.553554	Stable
0.25	0.4	0.5	0.7	0.7	0.4	0.4	0.6	0.15	0.1	2.96512	Stable
0.25	0.5	0.5	0.6	0.6	0.5	0.5	0.6	0.15	0.1	2.194286	Stable
0.25	0.6	0.5	0.5	0.5	0.6	0.6	0.6	0.15	0.1	1.25442	Stable
0.25	0.7	0.5	0.4	0.4	0.7	0.7	0.6	0.15	0.1	0.172767	Stable
0.25	0.8	0.5	0.3	0.3	0.8	0.8	0.6	0.15	0.1	-1.00768	Unstable
0.25	0.9	0.5	0.2	0.2	0.9	0.9	0.6	0.15	0.1	-2.2263	Unstable
0.25	1.0	0.5	0.1	0.1	1.0	1.0	0.6	0.15	0.1	-3.40298	Unstable
0.25	1.0	0.5	0.0	0.0	1.0	1.0	0.6	0.15	0.1	-0.42935	Unstable

4.1   Discussion of result

Table 4.1 shows the result of stability analysis of the disease free equilibrium state according to Bellman and Cooke [1]. The disease free equilibrium state will be stable only when the contraction rate β is low, effective application of anti retroviral drugs thus bringing down γ, high recovery from the latent classes thus increasing ε and ψ else we will have an unstable disease free equilibrium state.

5   Conclusion

From the stability analysis carried out it became obvious that Nigeria is a stable Tuberculosis endemic nation. If Nigeria is to maintain the present condition we will never be able to eradicate tuberculosis from Nigeria. The non availability of data on Latent TB treatment poses a serious threat that millions of Nigerians infected with Latent TB are out there waiting for any possible immunosuppressive condition that will break them down to Infectious TB.

The fact that TB is an air borne disease made it possible for a single infectious TB patient to infect hundreds of Susceptible individuals even before commencement of treatment thereby moving them into latent class and if these cases remained untreated, any compromise of their immune system will push them into the infectious class.

5.1   Recommendations

Nigeria is in a very critical situation. Efforts should be intensified to move the nation out of the current endemic situation to a stable disease free nation. This can be achieved by committing more effort and resources into detecting and treating Latently infected individuals, reducing the break down of immune system of HIV patients by procurement of Antiretroviral drugs, immediate isolation and commencement of treatment of Infectious TB cases and so on. Tuberculin Skin Test should be administered to all contacts of an infectious TB case. Isoniazid preventive therapy should be administered to those positive to Tuberculin Skin Test.

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