Mathematical Model to Simulate Tuberculosis Disease Population Dynamics

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Abstract: A mathematical model to depict Tuberculosis disease population dynamics was presented. The model population was compartmentalised as appropriate and the resulting model equations were solved numerically while different instances of the disease transmission were simulated. The graphical profiles of the various sub-populations with time were presented and discussed based on the results from our simulations. Also, the disease-free and endemic equilibrium of the system were established and analyzed for stability.

Keywords: Mathematical Model, Tuberculosis (TB), Directly Observed treatment Strategy (DOTS), Bacillus Calmette-Guerin (BCG), Stability analysis

INTRODUCTION

Tuberculosis (TB) is a contagious bacteria disease caused by inhaling the tubercle bacillus in the droplet nucleus form. Like the common cold, it spreads through the air. An infected person may have latent TB infection or active TB infection. Only actively infected people who are sick with TB bacilli in their lungs are infectious. When infectious people cough, sneeze, talk or spit, they propel TB germs, known as bacilli, into the air. A person needs only to inhale a small number of these to be infected [5]. A latent TB infected person does not show any symptoms of the disease and cannot infect others, though may live as long as possible without it degenerating into active TB.

Presently, the only effective vaccine for TB is Bacillus Calmette-Guerin (BCG) which is usually given to infants. This vaccine has a demonstrated efficacy ranging from no protection to 80% protection though a meta-analysis estimated that the overall efficacy of BCG is 50% [1]. However, due to case reports of disseminated BCG infection, where the vaccine is contraindicated in immunocompromised persons; safer and more efficacious vaccines are clearly needed [1].

Christopher Murray [4], Harvard School of Public Health, described a mathematical model developed to forecast the future impact of improvements in TB prevention and control. Specifically, this model projected the number of TB cases and deaths averted through the year 2050. Different scenarios were simulated to project the effect of adding TB vaccines to existing interventions. Six specific scenarios assessed the effect of vaccines (with efficacy levels of 20%, 50%, and 80%) to protect from *M. tuberculosis* infection, as well as the effect of vaccines of the same levels of efficacy to protect latently infected persons from "breakdown" to active TB. Although a TB infection vaccine with 20% efficacy would prevent more than 30 million TB cases, the best protection is obtained from a TB breakdown vaccine with 80% efficacy, which would prevent almost 130 million TB cases. The breakdown vaccine could be used in the large number of persons with latent *M. tuberculosis* infection, now estimated at almost one third of the world's population. Such anticipated gains justify the effort to develop better TB vaccines.

In a related research work by Gammaitoni and Nucci [3], where mathematical model was used to evaluate the efficacy of TB control measures, it was found that environmental control cannot eliminate the risk of TB transmission during high-risk procedures; respiratory protective devices, and particularly high-efficiency particulate air masks may provide nearly complete protection if used with air filtration or ultraviolent irradiation, although the efficiency of these control measures decreases as the infectivity of the source case increases; while administrative control measures are the most effective because they substantially reduce the rate of infection.

In another research work conducted by Dye et al [2], they developed a mathematical model that makes use of routinely-collected data to calculate the number of

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deaths directly prevented by TB treatment. The method was applied to the world largest TB control programme covering over 500 million people in 12 provinces in China. Their results showed that counties which had enrolled in the programme since 1991 were, by 1997, preventing at least 46% of the TB death that would have otherwise occurred. They concluded that the short-course chemotherapy has substantially reduced TB mortality in half of China.

According to the work of Castro [1], the effect of the HIV epidemic on TB has been major in Africa, where HIV seroprevalence among TB cases is 50% to 70% and TB case notifications have at times tripled. However, countries with inadequate TB control are particularly exposed to the consequences of both epidemics. Moreover, he found out that TB remains an important public health problem in many areas of the world where direct observation treatment short-course (DOTS) has not been implemented because treatment outcomes were better in countries where DOTS has been used, though he averred that the strategy needs to be expanded rapidly and new tools to facilitate its implementation need to be developed.

The co-pandemic nature of TB-HIV calls for more quantitative research work on TB particularly because it has cure unlike HIV. It should then be no surprise that mathematical models are now been deployed in the study of the disease epidemiology and the evaluation of some of the world TB control measures and strategy. Thus, if we are able to reduce(to barest minimum) the spread of TB via all the control measures and strategies, we will have succeeded in reducing the alarming TB death tools and increase the life expectancy of HIV patients by reducing their chances of contacting TB, which may lead them to early grave.

In this paper, we will present a mathematical model for the Tuberculosis disease population dynamics using Susceptible-Infected-Recovered but Susceptible (SIRS) model which is different from the approaches used in some the cited paper, though results may be interrelated and can help to confirm or refute the earlier findings. Moreover, we shall evolve appropriate system of equations and solve the equations numerically. Also, we will simulate different instances of the infected sub-population base on the effect of the different TB control measures and strategy. Finally, we shall establish the model system equilibriums and analyse their stability.

Model Formulation: Based on the standard SIRS model, the model population was compartmentalised into the susceptible (S) and the infected (I) which is further broken down into latently infected (I_L) and actively infected (I_A) while the recovered sub-population is ploughed back into the susceptible group due to the possibility of re-infection after successful treatment of the earlier infection. The model monitors the temporary dynamics in the population of susceptible people S(t), TB latently infected people I_L(t) and TB actively infected people I_A(t) as captured in the model system of ordinary differential equations that follows:

$$\left.\begin{array}{l} \dfrac{dS}{dt} = nfN - aI_A S - dS + T_A I_A + T_L I_L \\[2mm] \dfrac{dI_L}{dt} = (1-p)aI_A S - b_A I_L - T_L I_L - dI_L \\[2mm] \dfrac{dI_A}{dt} = p\,aI_A S + b_A I_L - T_A I_A - dI_A - eI_A \\[2mm] S(0) = N, I_L(0) \geq 0, I_A(0) \geq 0. \end{array}\right\} \quad (2.1)$$

The model parameters and their respective descriptions are given in the table below:

Table 1: Model parameters and their interpretations

Parameter	Description
N	Total number of new people into the location of interest
S	Number of susceptible people in the location
I_L	Number of TB latently infected people
I_A	Number of TB actively infected people
?	Probability that a susceptible person is not vaccinated
f	Efficacy rate of vaccines
T_L	Success rate of latent TB therapy
T_A	Active TB treatment cure rate
a	TB instantaneous incidence rate per susceptible
d	Humans natural death rate
p	Proportion of infection instantaneously degenerating into active TB
e	TB-induced death rate
$ß_A$	Breakdown rate from latent to active TB

As can be observed from (2.1), the susceptible population changes due to the coming of new susceptible people into the population (nfN) where we assumed that people come into the location of interest at a constant rate N and this is further increased by the people who are cured from active TB and those successfully treated for latent TB while the susceptible population diminishes due to natural death at d death rate and infection with a incidence rate of infection.

The instantaneous incidence rate of infection (a) per susceptible will depend on number of respiratory contact with infection per susceptible people and the probability that the contact lead to TB infection

In same way, the latently infected population dynamics depends on the proportion of the TB infection that resulted in latent TB infection ($(1-p)aI_AS$) and this is reduced by loss due to natural death , successful treatment of latent TB patients, and occasional breakdown of latent TB infection into active TB infection.

Finally, the change in the actively infected TB population is dependent on the proportion of TB infection of the susceptible sub-population degenerating instantaneously into active TB infection plus the number of latently infected people breaking down into active TB patients while this is diminished due to natural death, successful cure of active TB patients, and death caused as result chronic active TB infection.

It is important to note that in this model, we assumed that successfully treated latent TB patients and cured active TB patients becomes susceptible immediately after their treatments whenever they are expose to TB infection again irrespective of their TB infection history. Realistically, this group may sometimes enjoy some temporary immunity to TB 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.

Equilibrium Analysis: Modelling infectious diseases demands that we investigate whether the disease spread could attain a pandemic level or it could be wiped out. The equilibrium analysis helps to achieve this. Thus, we shall consider the two equilibriums - the disease-free equilibrium and endemic equilibrium.

At equilibrium, the LHS of the three equations constituting the system of equation are zeros, i.e.

$$\frac{dS}{dt} = 0, \frac{dI_L}{dt} = 0, \frac{dI_A}{dt} = 0.$$

Hence, the system of equation becomes:

$$\left. \begin{array}{l} nfN - aI_AS - dS + T_AI_A + T_LI_L = 0 \\ (1-p)aI_AS - b_AI_L - T_LI_L - dI_L = 0 \\ paI_AS + b_AI_L - T_AI_A - dI_A - eI_A = 0 \\ S(0) = N, I_L(0) \geq 0, I_A(0) \geq 0. \end{array} \right\} (3.1)$$

Obviously, at the disease-free situation $I_L = 0$, and $I_A = 0$.

Thus, from equation (3.1) we have $nfN - dS = 0$.

$$\Rightarrow S = \frac{nfN}{d} = N^0$$

So, the disease-free equilibrium is $(N^0, 0, 0)$ However, for the endemic equilibrium, we solve equation (3.1) for S, I_L , and I_A respectively. This gives

$$S = \frac{nfN + T_AI_A + T_LI_L}{d + aI_A} = S^*,$$

$$I_L = \frac{(1-p)aI_AS}{b_A + T_L + d} = I_L^*,$$

$$I_A = \frac{b_AI_L}{T_A + e + d - paS} = I_A^*.$$

Thus, we can take our endemic equilibrium as (S^*, I_L^*, I_A^*) .

To test for the stability of each of the two equilibriums where we examine the behaviour of the model population near the equilibrium solutions (the disease free and the endemic), we need to linearize system of equations (2.1) by taking the Jacobian matrix of the system . For our system of equation (2.1), the Jacobian matrix is

$$J = \begin{bmatrix} -(aI_A + d) & T_L & T_A - aS \\ (1-p)aI_A & -(b_A + T_L + d) & (1-p)aS \\ paI_A & b_A & paS - (T_A + e + d) \end{bmatrix}.$$
(3.2)

At the disease-free equilibrium $(N^0, 0, 0)$, the Jacobian matrix becomes:

$$J^0 = \begin{bmatrix} -d & T_L & T_A - aN^0 \\ 0 & -(b_A + T_L + d) & (1-p)aN^0 \\ 0 & b_A & paN^0 - (T_A + e + d) \end{bmatrix} (3.3)$$

We shall now obtained the eigenvalues of J^0 as below

$$\begin{vmatrix} -(d+l) & T_L & T_A - aN^0 \\ 0 & -(b_A + T_L + d + l) & (1-p)aN^0 \\ 0 & b_A & paN^0 - (T_A + e + d + l) \end{vmatrix} = 0$$

(3.4)

Hence, the eigenvalues are
$l_1 = -d, l_2 = -(b_A + T_L + d), l_3 = T_A + e + d - paN^0$.

Obviously, $l_1 < 0, l_2 < 0$, but $l_3 < 0$ iff

$T_A + e + d < paN^0$ since all the model parameters
are positive.

The implication of the negativity of all the eigenvalues
of the system Jacobian is that disease free equilibrium
is stable and this so as long as $T_A + e + d < paN^0$
holds.

Similarly, for the endemic equilibrium $\left(S^*, I_L^*, I_A^* \right)$.
The associated Jacobian matrix is

$$J^* = \begin{bmatrix} -aI_A^* d & T_L & T_A - aS^* \\ (1-p)aI_A^* & -(b_A + T_L + d) & (1-p)aS^* \\ paI_A^* & b_A & paS^* - (T_A + e + d) \end{bmatrix}$$

(3.5)

Obtaining the eigenvalues as usual from
$|J^* - lI| = 0$. Results in characteristics polynomial

of the form $-l^3 + a_1 l^2 + a_2 l^1 + a_3 = 0$ where

a_1, a_2, a_3, depend the various combinations of the
model parameter values. In this case, the three
eigenvalues could all be negative, positive, zero, or any
combinations of the three alternatives. Thus, the
endemic equilibrium could be stable, unstable, or
saddle depending on the values of the various model
population parameters combined at a given time.

RESULTS AND DISCUSSION

The system of equation (2.1) was solved numerically
using maple mathematical package. The hypothetical
value for each of the model population parameters is as
given in the table that follows:

Table 2: Hypothetic values of each model parameters
used for the numerical solution.

Parameter	Values
N	100
?	0.9
f	0.50
T_L	0.8
T_A	0.74
a	0.41
d	1/(365x 70)
p	0.00196
e	0.0735
ß$_A$	0.01

The results from our numerical solutions are
displayed in the graphs that follow:
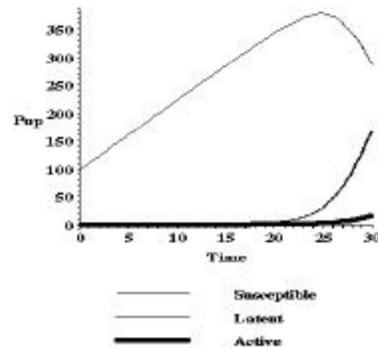
Fig.1:S(0)=99,I_L(0)=1,I_A(0).
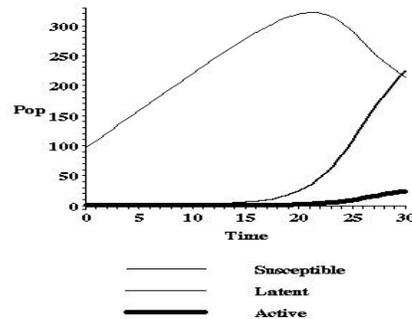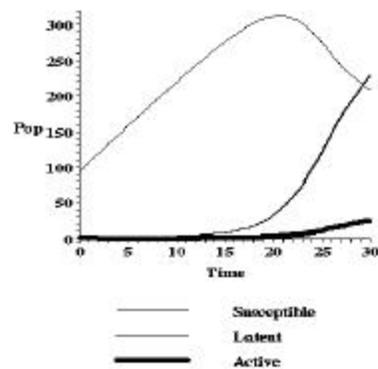

Fig. 2: S(0)=99, I_L(0)=0, I_A(0)=1,

Fig.3: S(0)=96, I_L(0)=3, I_A(0)=1.

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In Fig. 1-3 above, we solved the model equations and simulated for different initial conditions. The trivial case is when the initial condition were zeros for the latently and actively TB infected population, and for this we expect a steady rise in the susceptible with occasional drops while the infected (both latent and active) population remained at zero level. However, we did not bother to show the graph of this since it is obvious.

In Fig. 1, the TB spread starts with an latently infected patients, it takes sometime before the hitherto uninfected people in the environment gets infected, while in Fig. 2 the TB spread starts from an actively infected TB patients, the disease spread is very rapid leading to more latently infected people and less actively infected people. However, in Fig. 3 we considered a situation where the spread starts from both actively and latently infected TB patients, the results here shows no significant difference to the case when it starts from an actively infected patient except that the disease spread is slower in the latter.

In addition, we simulate our model equations for varying TB incidence transmission rates and below are the resulting graphs:
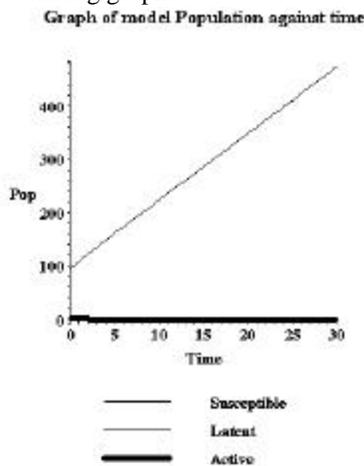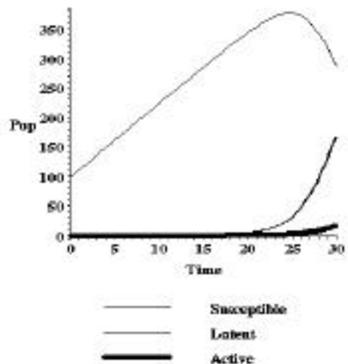

Fig. 4: Graphs of result for a=0.001
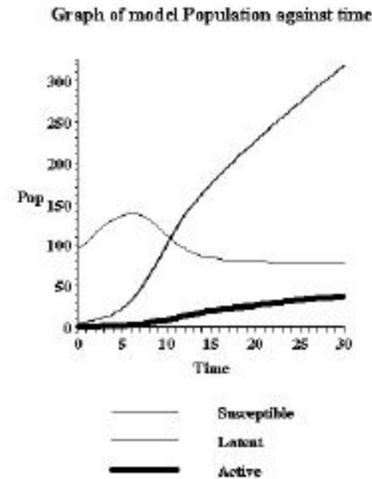

Fig. 5: Graphs of results for a=0.041

Fig. 6: Graphs of results for a=0.1

As can be seen from above graphs in Fig. s 4 to 6, the disease spreads more rapidly as the disease incidence transmission rate increases. Precisely, when the disease incidence transmission rate (a) is 0.001, meaning that one in every one thousand people that are exposed to the disease gets infected, the population of actively and latently infected remained close to zero all through. Moreover, when the disease incidence transmission rate (a) is 0.041, meaning that about four in every one hundred people that are exposed to the disease gets infected, the population of latently and actively infected people starts to increase departing from zero with the former increasing more rapidly. Nevertheless, for a situation with disease incidence transmission rate (a) equals 0.1, meaning that in every ten people that are exposed to the disease one gets infected, the disease spread more rapidly to the extent that within a short time, the number of latently infected people out-numbers the susceptible while the number of actively infected people approaches half the number of the susceptible. The inference that could be drawn from the above is that the spread of the disease can be drastically reduced if we can put in place measures and controls that will reduce the disease incidence transmission rate. Thus, any measures that will reduce either the respiratory contact with infection per susceptible or the probability that the contact leads to infection will help check the spread of the disease. Hence, this also confirms the findings of Gammaitoni and Nucci[3] which asserts that administrative control measures are the most effective since they are capable of reducing the disease incidence transmission rate to as close as possible to zero.

CONCLUSIONS

In this research work, we considered the dynamics of the Tuberculosis disease population using the SIRS model. The resulting model equations were solved numerically and results were presented graphically based on our simulations. Our results show that the population dynamics depends more on the number of actively infected people in the population at the initial time and also on the disease incidence transmission rate at a given time. Most importantly, we also showed that the disease-free equilibrium is stable while the endemic equilibrium may or may not be stable depending on the various values of the model parameters.

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