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A Simulation-Based Study of Tuberculosis Epidemic in Ibadan, South Western Nigeria

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Abstract

In this paper, we conduct a simulation experiment to assess the impact of vaccine on the number of tuberculosis (TB) infections in Ibadan, South Western, Nigeria. The analysis is based on a vaccine-dependent mathematical model for which we imputed reported TB data from 1998-2008 from all the treatment centers in Ibadan metropolis. Simulation was run for 10 years while Maple 18 was used for the computations. Simulation results showed a steady reduction in the number of infected and susceptible individuals for each year in the simulation with increasing levels of vaccine efficacy. The result of this paper provides useful tools in identifying population group at a higher risk of infection, assessing therapy strategies and estimating key parameters from TB data which in turn would aid policy decisions on TB prevention and control.

Keywords: Tuberculosis, mathematical model, simulation, vaccine efficacy, basic reproduction number.

1.0 Introduction

Tuberculosis (TB) constitutes the main burden of infectious disease in humans especially in developing countries [1, 2]. Estimates by the World Health Organisation indicate that there are more than 9 million new active cases of TB and close to 2 million deaths per year (WHO, 2010). Despite the widely implementation of WHO directly observed therapy, short course [3] and different TB control strategies, Mycobacterium TB infection continues to pose diagnostic and therapeutic challenges and exert immense pressure on health care systems in Africa and Asian countries with large populations of infected individuals [4]. This rise may be attributed to resurgence of multi-drug resistant TB strains, co-infection of TB and HIV and the collapse of public health programs in these regions [5, 6].

Global TB progress recently released showed that the number of cases of multi-drug resistant tuberculosis (MDR-TB) notified in the 27 high MDR-TB burden countries is increasing despite the Millennium Development Goal (MDG) target to halt and reverse TB epidemic by 50% [7]. Despite some successes associated with using TB drugs, vaccines and some TB prevention and therapeutic strategies, it is generally believed that there are critical gaps for TB care and control [8, 9]. New drugs and new vaccines are urgently needed to replace the old ones which only inhibit or delay TB reactivation [10]. New TB drugs and vaccines to prevent infection, achieve sterile eradication and treat all forms of TB should be designed to help combat the global spread of the epidemic.

Over the last few decades, mathematical models have been widely applied to study the dynamics of TB epidemic. The models have helped in understanding the interplay between variables that determine the course of TB infection, identifying the highest risk group of contacting the disease and predicting optimal treatment strategies needed to achieve TB prevention and control. In this paper, we develop a vaccination model for the epidemiology of TB. We simulate the model using reported TB infection data in Ibadan, South Western, Nigeria to show the efficacy of vaccine (e.g. Baccile Calmette Guerin) in reducing the populations of infected and susceptible individuals in the population. Simulation was carried out using Maple 18 [11].

2.0 Model Formulation

Let S, V, E, I, R. denotes the number of susceptible, vaccinated, exposed, infective and recovered class respectively. We partition the vaccinated compartment into five subclasses of vaccinated susceptible(V_S), vaccinated exposed (V_E), vaccinated

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infected (V_I), vaccinated protected (V_P) and vaccinated recovered (V_R) individuals. Then, the proposed model is given by

$$\frac{dS}{dt} = (1-\gamma)(1-n)\pi + qV - \beta IS - \mu S$$

$$\frac{dV}{dt} = n(1-\gamma)\pi - qV - (1-f_1)\beta IV/N - \mu V$$

$$\frac{dV_P}{dt} = n(1-\gamma)\pi - qV - (1-f_1)(1-f_2)\beta IV_p/N - \mu V_p$$

$$\frac{dV_S}{dt} = n(1-\gamma)\pi - qV - (1-f_1)\beta IV_s/N - \mu V_s$$

$$\frac{dV_I}{dt} = n(1-\gamma)\pi - qV - (1-f_1)\beta IV_I/N - \mu V_I$$

$$\frac{dV_R}{dt} = n(1-\gamma)\pi - qV - (1-f_1)\,\beta IV_R/N - \mu V_R$$

$$\frac{dV_E}{dt} = n(1-\gamma)\pi - qV - (1-\rho)\,(1-f_1)\beta IV_E/N - \mu V_E - vV_E \quad (1)$$

$$\frac{dE}{dt} = (1-\rho)\beta IV/N - (\mu+v)E + \rho\beta IE/N \; - \varepsilon E$$

$$\frac{dI}{dt} = dvE + \rho\beta IS/N + \; (1-f_1)(1-f_2)\beta IV/N - \quad (\mu+\mu_T+\varepsilon)I - sI$$

$$\frac{dR}{dt} = sI - \beta IR/N \; - \mu R$$

Using the approach of Diekmann and Heesterbeek [12], the basic reproduction number R_0, for the model is given by

$$R_0 = \frac{\beta[\mu(1-n)+q]\pi - (1-f_1)(1-f_2)}{\mu(\mu+s)(\mu+q)(\mu+\varepsilon)} \quad (2)$$

The detailed description of the model parameters are given in Table 1.

Table 1: Description of Parameters of the Model

Parameters	Description
π	recruitment rate
γ	proportion of recruitment due to migration
n	proportion of immigrants that are vaccinated
v	rate of slow progression
ρ	rate of fast progression
μ	natural death rate
μ_T	death rate due to TB
β	transmission rate
d	detection rate of active TB
s	treatment rate of active TB
ε	recovery rate from active TB
q	rate of waning of vaccine
f_1	efficacy rate of vaccine in preventing initial infection
f_2	efficacy rate of vaccine in preventing fast progressive to active TB

3.0 Numerical Simulations

The proposed model was fitted to 10 years TB data from all the 5 LGA's in Ibadan metropolis. The data used for the study

was obtained from the local TB treatment centers. The model was simulated for each year using the reported TB prevalence (Table 2) as the initial amount of total active TB in the population. We imputed year-specific detection and treatment rates (Table 3) for each simulation and all simulations run for 10 years. Parameter values were drawn from the TB literature wherever possible (Table 4), otherwise they were assumed.

Simulation results showing the proportion of $S, I, V, E, V_P, V_I, V_S$ for each year of simulation are captured in figures 1-2. Simulation was done for the two variants of the disease: disease-free equilibrium and endemic equilibrium. Maple 18 was used for the computations.

In Table 2, TB indicators are obtained from treatment centres. "inc" denotes the incidence of active TB which is the number of new TB cases in a year. "Prev" is the total number of active TB infection in a year. Both indicators are reported per 1000 population.

Table 2: Incidence and Prevalence rates of TB in Ibadan Metropolis

Year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
inc	2.48	2.47	2.44	2.45	2.43	2.42	2.41	2.40	2.41	2.40	2.39
Prev	1.63	1.61	1.60	1.60	1.59	1.58	1.57	1.57	1.56	1.56	1.52

Source: TB Treatment centres in Ibadan metropolis

In Table 3, we have TB indicators showing detection and treatment rates. We use WHO indicator whole country all new cases detection rate, $d = \frac{inc}{N}$ (where $N = 1000$). The treatment success rate is denoted by s. We use WHO treatment success rate WHO [8] given by the formula $s = d \times \frac{inc}{Prev}$.

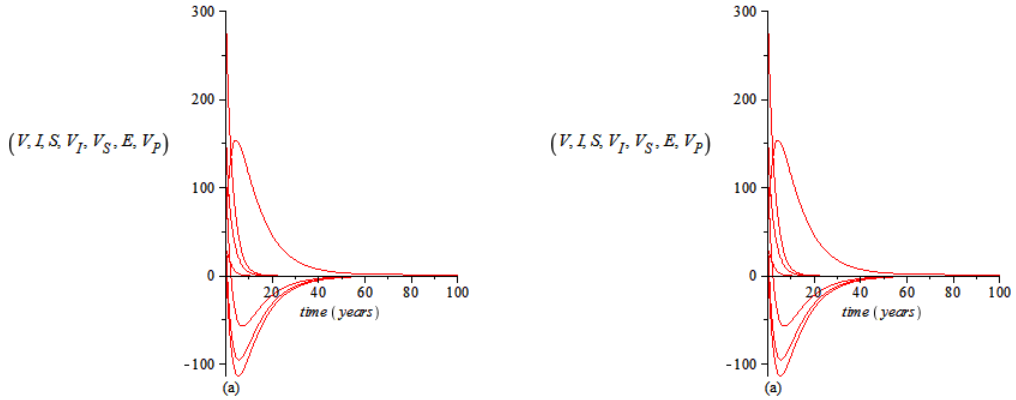
Table 3: Detection and Treatment rates of TB in Ibadan Metropolis

Year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
d	0.25	0.25	0.24	0.24	0.23	0.26	0.24	0.24	0.25	0.24	0.26
s	0.38	0.38	0.37	0.38	0.35	0.39	0.37	0.37	0.36	0.37	0.40

Table 4: Parameter values used for the simulations

Parameters	Range	Reference
π	[0.2, 0.6]	Assumption
n	[0.1, 0.3]	Assumption
v	[0.002, 0.004]	[13]
μ_T	[0.0025, 0.0042]	Assumption
μ	0.1	[14]
ρ	[0.0050, 0.0098]	[14]
β	[0.238, 0.349]	[13]
γ	[0.3, 0.5]	Assumption
q	[0.24, 0.36]	Assumption
f_1	[0.1]	Assumption
f_2	[0.1]	Assumption
ε	[0.14, 0.5]	[14]

4.0 Results



Parameter values were chosen as follows: $f_1 = 0.09, f_2 = 0.01, \gamma = 0.3,$ $n = 0.1, \pi = 0.2, q = 0.24, \mu = 0.1, v = 0.002, \rho = 0.005, \beta = 0.238,$ $\mu_T = 0.0025, \epsilon = 0.5, d = 0.25, s = 0.38$

DISEASE-FREE EQUILIRIUM

Parameter values were chosen as follows: $f_1 = 0.09, f_2 = 0.01, \gamma = 0.3,$ $n = 0.1, \pi = 0.2, q = 0.24, \mu = 0.1, v = 0.002, \rho = 0.005, \beta = 0.238,$ $\mu_T = 0.0025, \epsilon = 0.5, d = 0.25, s = 0.38$

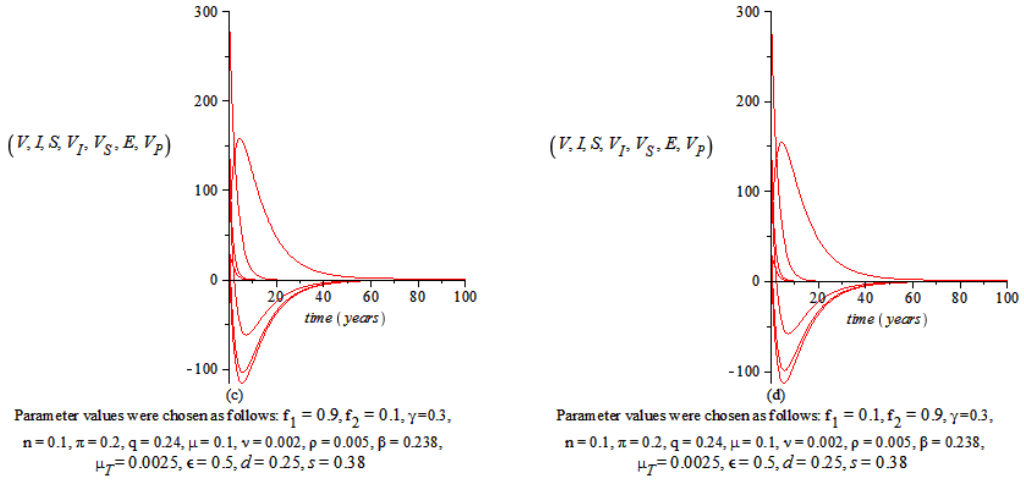


Figure 1: TB Simulations for disease- free equilibrium showing the proportion of the population that is actively infectd. In each graph, we assume different levels of vaccine efficacies while fixing other parameters.

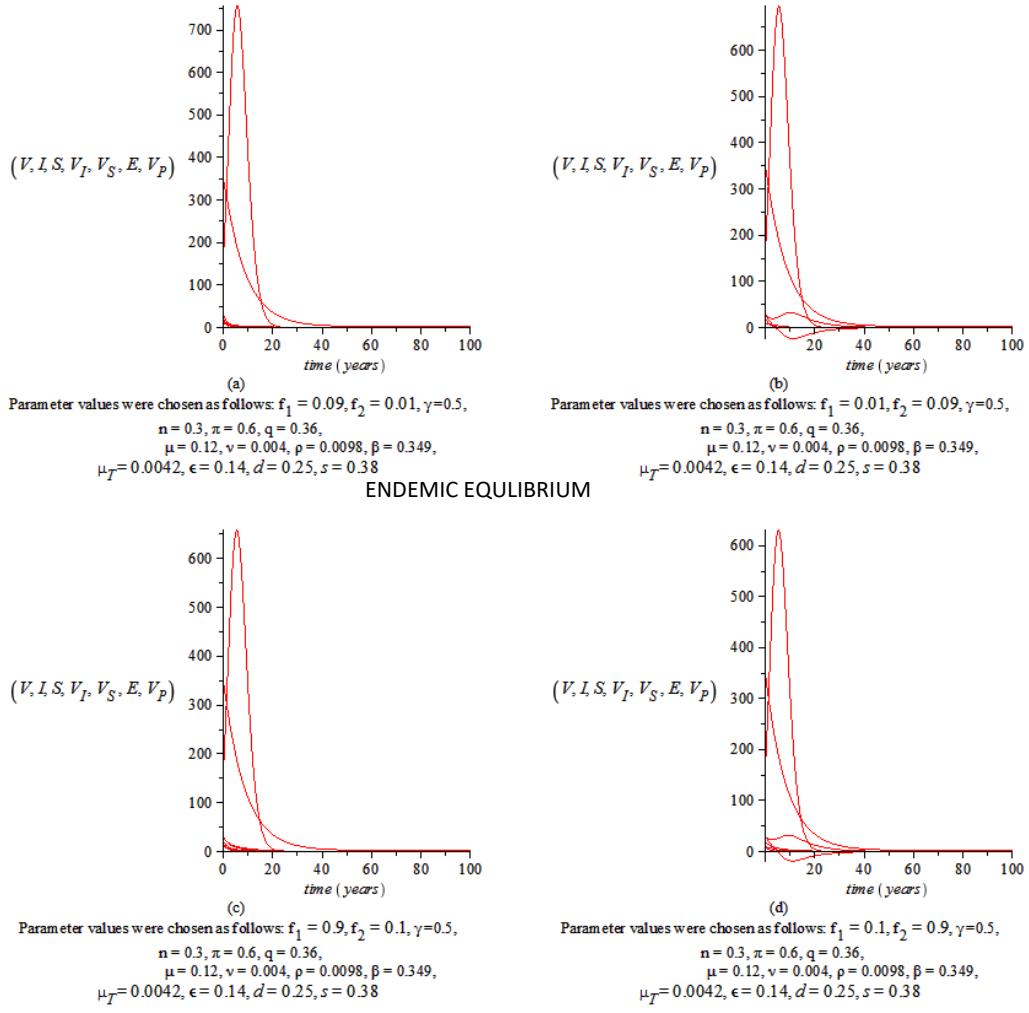


Figure 2: TB Simulations for endemic equilibrium showing the proportion of the population that is actively infected. In each graph, we assume different levels of vaccine efficacies while fixing other parameters.

5.0 Discussion of Results and Conclusion

In figure1, simulation results showed a steady reduction in the number of infected and susceptible individuals for each year. This means that increasing the levels of vaccine efficacy would bring a more stable disease-free equilibrium for eradication of TB disease. It is also apparent from the figure that 20 years mass vaccination will be very likely beneficial since all TB infections die out during the 20 years period. Furthermore, simulations show that the number of infective decreases with increasing vaccine efficacies. Another interesting feature is that the number of years for infection to go into extinction is reduced when vaccine efficacy levels are varied. For instance, if $f_1 = 0.01$ and $f_2 = 0.09$, elimination year of TB is projected to occur in 18 years while the infection is cleared in 13 years if $f_1 = 0.1$ and $f_2 = 0.9$.

Considering endemic equilibrium, figure 2 showed that the number of new TB infections increases in the initial years of simulation before it gradually decreases. This suggests the effectiveness of the vaccine in the treatment of TB disease. From the figure, elimination of TB can be achieved between 25-30 years. Moreover, nearly in all simulations, it is observed that increasing the relative efficacy of vaccine (f_1&f_2) plays a significant role in reducing the number of infective and its proportion to the total population. This indicates that larger values of f_1 and f_2 would make the endemic equilibrium unstable and decrease the number of new infections so that disease eradication may be achieved in finite time.

In conclusion, these results suggest that active tuberculosis must be treated with vaccination at a fairly high rate especially in high TB burden countries like Nigeria to ensure a steady reduction in the number of infected and active tuberculosis cases.

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