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Effects of Vaccine Efficacy on Basic Reproduction Number of a Vaccination Model of Tuberculosis.

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Abstract

This paper addresses the effect of vaccine efficacy rate on a vaccination model of tuberculosis (TB) epidemic. Numerical simulations was performed on the model using

Maple 15 computation software. Our results showed that as the levels of vaccine efficacy increase, the basic reproduction number, R_0, decreases. This implies that if the protective effect of TB vaccine is increased, it would bring a lower R_0. In consequence, there would be a steady reduction in the number of infectives and susceptibles while eradication of infection would be achieved in finite time. Graphical results are also presented and discussed qualitatively.

Keywords: Mathematical model, tuberculosis, basic reproduction number, vaccine efficacy, equilibrium points, stability.

1.0 Introduction

Tuberculosis (TB) is an infectious disease which can be fatal [1]. It is an airborne disease caused by Mycobacterium tuberculosis which primarily affects the longs. The primary stage of TB does not cause symptoms. Left untreated, an infected person can spread the germs to about 10-15 people every year [2]. Symptoms of TB include chest pain, weight loss, loss of appetite, fever, night sweat, presence of blood in cough and sneezing [3]. TB treatment requires a longer course of treatment between 6 to 9 weeks. The goal of treatment is to cure infection with drugs that fight the TB bacteria. Commonly used drugs include Isoniazid, Rifampin, Pyrazinamine, Amikacin, Ethionamide and Rifanpicin [4].

TB disproportionately affects people in resource-poor settings particularly in Africa and Asia where it poses enormous threat to their economies since it mostly affects young adults in their most economically productive years [5]. Despite successful implementation of various strategies on TB treatment, the global burden of TB remains enormous. An estimated 14 million people worldwide are infected with active TB [6]. In 2009 alone, there were 9.4 million new cases of TB while 380,000 out of 1.7m reported deaths were related to TB among people with HIV [7]. In 2011, 8.7million people suffered from TB related illnesses leading to 1.4 million deaths. According to the report of WHO in November 2010, impressive progress has been made towards global reductions in TB incidence. The number of new TB cases is on the decline worldwide with the exception of Southern Asia and Africa.

The epidemiology of TB varies substantially around the world. The highest rate of 100 per 100,000 populations is observed in sub-Sahara Africa, India, China and Asia. Estimates provided by USAID in 2007 for South Sudan were 228 cases per 100,000 populations. Nigeria had 210,000 new cases of TB in 2010 which is equivalent to 133/100,000 populations [8]. A report by the United States Embassy in January 2012 showed that Nigeria is ranked 10th among the 22 high-burden TB countries in the world. The TB burden in Nigeria is compounded by a high prevalence of HIV in the country, limited laboratory capacity for case detection and treatment barriers and complications and the emergence of multi-drug resistant TB. Mathematical models have been widely used in different forms to gain significant insights into TB dynamics.

From the work of Okuonghae [9], despite the implementation of WHO directly observed therapy short course (DOTS) programme in Nigeria, eradication of TB may not be feasible if the fraction of detected infected individuals do not exceed a critical value that could result into a globally stable disease-free equilibrium. He concluded that DOTS expansion must include significant increase in the detection rate of infected individuals to reduce TB incidence in Nigeria.

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In Long et al [10], a model of HIV-TB infection in India was developed. Both numerical and qualitative analyses of the model were done and the effects of hypothetical prevention and treatment strategies were investigated. Their analysis suggests that co-ordinated treatment effects that include highly active antiretroviral therapy for HIV, latent TB prophylaxis and active TB treatment may be necessary to slow HIV-TB co-epidemic.

Adetunde [11] reviewed a mathematical model of TB in Ghana. The equilibrium points of the model were found and their stability was investigated. His model exhibited two equilibria namely the disease-free equilibrium (DFE) and endemic equilibrium. He used stability theory and computer simulations and noted that population size determines the rate of TB infection. The higher the population density, the greater the instability of the DFE and the greater the risk of the spread of the disease.

According to White and Garnett[12], many aspects of natural history and transmission dynamics of TB were still not fully understood as was reflected in the differences in the structures of mathematical models of TB. The authors concluded that gaining a greater understanding of TB epidemiology would require further empirical laboratory and field work, mathematical modeling and interaction between them.

Claude et al.[13] studied the spread of TB through one-strain and two-strains models. They first presented a model that incorporated fast and slow progression, effective chemoprophylaxis and therapeutic treatment. They proved that if the basic reproduction number R_0 equals one ($R_0 = 1$), the DFE is globally asymptotically stable (GAS) and if $R_0 > 1$, an endemic equilibrium exist which is also GAS. The second model dealt with the problem of drug resistant TB. Their objective was to characterize the role of multi-drug resistant in the dynamics of TB. They discussed the existence and stability of the associated equilibria of the model.

Egbetade and Ibrahim [14] formulated a mathematical model of TB infection and conducted global stability of the two equilibrium states of their model. Using Lyapunov functions and Volterra-Lyapunov matrix properties, they proved global stability of the DFE and endemic equilibrium.

Li and Cui [15] studied the behaviour of a discrete-time SIS model with non-linear incidence rate which was appropriate for TB dynamics. The theoretical analysis and numerical simulations of the model demonstrated that the model exhibits a variety of dynamical behaviours such as backward bifurcation, hopf bifurcation, flip bifurcation and chaos.

Recently, Gyasi-Agyei et al. [16] presented a model which fits into TB occurrence data of Ashanti Region of Ghana. In their analysis, they found that TB occurrence in the region can best be modeled with a stochastic time series linear model (ARMA(1,0) or AR(1)) and predicted that TB epidemic in the region would be stable between April 2013 and April 2015.

2.0 The Model

We shall consider the differential system that describes the TB dynamics which is proposed by Egbetade et al. [17].

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

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

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

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

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

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

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

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

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

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

The detailed description of the variables and parameters of the model are given in Tables 1 and 2

Table 1: Description of Variables for the Model

Variable	Description
Tab	
Vari	
S	susceptible individuals
V	vaccinated individuals
V_P	vaccinated protected individuals (i.e. fully protected from acquiring TB)
V_S	vaccinated susceptible individuals
V_E	vaccinated exposed individuals
V_I	vaccinated infected individuals
V_R	vaccinated recovered individuals
E	exposed or latently infected individuals
I	actively infected individuals
R	recovered individuals

Table 2: Description of Parameters for the Model

Parameters	Description
π	recruitment rate into the population
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	waning rate of the vaccine
f_1	efficacy of vaccine in preventing initial infection
f_2	efficacy of vaccine in preventing fast progression to active TB.

Following the approach of Diekmann and Heesterbeek [18] for calculating the basic reproduction number R_0, for R_0 for the model is given by

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

Stability

Linearising the model near the DFE and using stability theories gives the DFE point A_0 given by

$$A_0 = (S_0, V_0, V_{P_0}, V_{S_0}, V_{I_0}, V_{R_0}, V_{E_0}, E_0, I_0, R_0)$$
$$= \left(\frac{(1-\gamma)[\mu(1-n)+q]\pi}{\mu(\mu+q)}, \frac{n\pi(1-\gamma)}{\mu+q}, \frac{n\pi(1-\gamma)}{\mu+q}\right.$$
$$\left.\frac{n\pi(1-\gamma)}{\mu+q}, \frac{n\pi(1-\gamma)}{\mu+q}, \frac{n\pi(1-\gamma)}{\mu+q}, \frac{n\mu\pi(1-\gamma)}{(\mu+q),(\mu+v)}, 0, 0, 0\right)$$

which is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$. The endemic equilibrium $A^* = (S^*, V^*, V_P^*, V_S^*, V_I^*, V_R^*, V_E^*, E^*, I^*, R^*)$ should always be positive since the model monitors human population and is globally asymptotically stable (GAS) when $R_0 > 1$ (see ref [17]).

3.0 Numerical Simulations

Within the framework of our mathematical model, the basic reproduction number R_0 is the total number of new infections that an average infectious individual will induce in a completely susceptible population. Toassess the impact of vaccine efficacy (f_1, f_2) on R_0, numerical simulations was performed using model parameters for the disease-free equilibrium and endemic equilibrium. Since no vaccine protects completely, we vary f_1, f_2 in the range [0.01, 0.9]. All other parameters are also varied to show the two equilibrium states of the model. From the figures, we display results of the basic reproduction number R_0 as a function of vaccine efficacy rates f_1, f_2 for the model's equilibria. Maple15 software package[19] was used for the simulations.

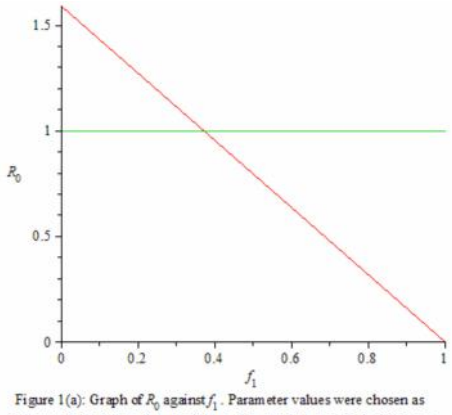

Figure 1(a): Graph of R_0 against f_1. Parameter values were chosen as follows: β =0.238, μ =0.1, n =0.1, π =0.2, q =0.24, ε =0.5, f_2 =0.01, s = 0.38

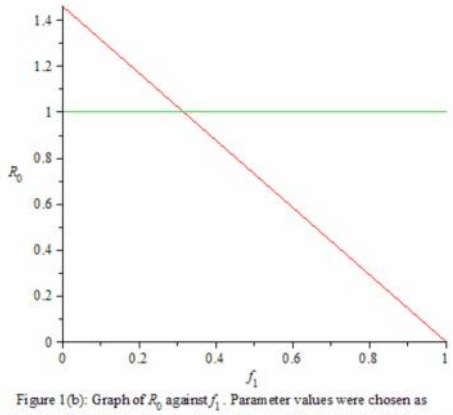

Figure 1(b): Graph of R_0 against f_1. Parameter values were chosen as follows: β =0.238, μ =0.1, n =0.1, π =0.2, q =0.24, ε =0.5, f_2 =0.09, s = 0.38

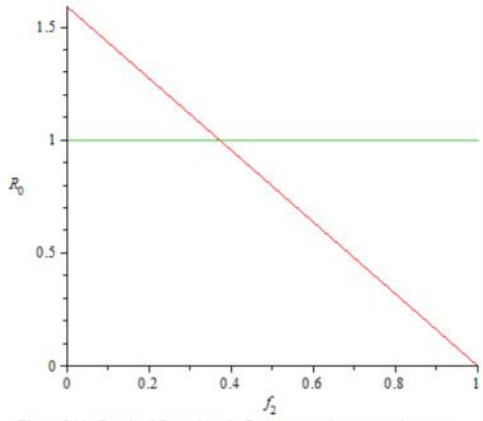

Figure 2(a): Graph of R_0 against f_2. Parameter values were chosen as follows: β =0.238, μ =0.1, n =0.1, π =0.2, q =0.24, ε =0.5, f_1 =0.01, s = 0.38

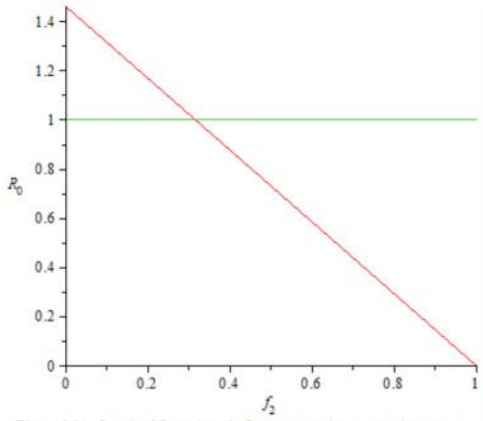

Figure 2(b): Graph of R_0 against f_2. Parameter values were chosen as follows: β =0.238, μ =0.1, n =0.1, π =0.2, q =0.24, ε =0.5, f_1 =0.09, s = 0.38

4.0 Discussion of Results

Comparing figures 1(a) and 1(b), it could be observed that as the efficacy of the vaccine in preventing against initial infection (f_1)is increased from 0.01 to 0.09 the basic reproduction number (R_0)which determines whether an infection will occur or not decreases from 1.5 to 1.4. A similar result is obtained in figures 2(a) and 2(b) where we increase vaccine efficacy in slowing down progression to active TB (f_2)from 0.01 to 0.09. These results indicate that vaccine efficacies play significant role in controlling the basic reproduction number of TB transmission. From the figures, as the levels of vaccine efficacy is increasing, R_0 decreases to values below 1, thus making the DFE more stable while the endemic equilibrium loses its stability. This would ensure that the infection dies out in time. Furthermore, the results suggest that increasing the relative efficacy of TB vaccines like Bacille Calmette Guerin (BCG) could bring reduction in the number of infective and susceptible individuals due to the effect of the vaccine in lowering $R_0$and consequentlyslow down the growth rate of infection.

5.0 Conclusion

We have used a novel TB model to assess the impact of vaccine efficacy on TB transmission dynamics. Our analysis showed that if a TB vaccine is highly efficacious then it would result in lowering the basic reproduction number (R_0) and slow down disease progression to ensure reduction or eradication of infection in finite time. However, there is strong need for the development of new vaccines to replace the last generation vaccines which efficacy against pulmonary TB in adults is inconsistent and incomplete. The old vaccines only inhibit or delay TB re-activation and cannot fight drug-resistantor drug-sensitive strains of Mycobacterium tuberculosis. Owing to these short comings, new vaccines which aim at preventing infection or achieve sterile eradication should be developed. The World Health Organisation (WHO) and all other allied bodies should accelerate efforts at developing new drugs and vaccines to improve both vaccination and drug therapy of TB.

6.0 References

[1] Canadian Centre for Occupational Health and Safety (2012).CCHS. Available on line at: www.cchs.caloshanswers/disease/tuberculosis.html

[2] World Health Organisation (2009). Global tuberculosis control. Available on line at: http://who/global/report 2009/pdf/

[3] Bowong, S. and Kurths, J. (2012). Modeling and analysis of the transmission dynamics of tuberculosis without and with seasonality. *Nonlinear Dynamics* 67, 2027-2051.

[4] USAID (2007). United States Agency for International Development. Global tuberculosis report. Available on line at: http://www.usaid/globaltbreport/

[5] World Health Organisation (2011). The global plan to stop TB. Available on line at: http://www./stop tb.org/global/plan/

[6] World Health Organisation (2013). Global tuberculosis report. Available on line at: http://who/globaltbreport 2013/pdf/

[7] World Health Organisation (2010). Tuberculosis fact sheet. Available on line at: http://www.who.int/medicentre/fact sheet/ html

[8] World Health Organisation (2012). Global tuberculosis report. Available on line at: www.who.int/tb/publications/factsheet global.pdf.

[9] Okuonghae, D. and Korobeinkov, A. (2007). Dynamics of tuberculosis: The effect of Direct Observation Therapy Strategy (DOTS) in Nigeria. *Epidemiology* 2(1), 101-113.

[10] Long, E.F., Validya, N.K. and Brandeau, M.L. (2008). Controlling Co-epidemics: Analysis of HIV and Tuberculosis infection dynamics. *Operations Research* 56(6), 1366-1381.

[11] Adetunde, I.A. (2009). The mathematical models of the dynamical behaviour of tuberculosis disease in the upper East Region of the Norther Part of Ghana: A case study of Bawlcn. *Current Research in Tuberculosis* 1, 15-20.

[12] White, P.J. and Garnett, G.P. (2010). Mathematical modeling of the epidemiology of tuberculosis. *Adv. Exp. Med. Biol.* 673, 127-140.

[13] Claude, J.K., Bowong, S. and Jean, J.T. (2011). Stability analysis of the transmission dynamics of tuberculosis models. Available on line at: www.worldacademic union com/journal.1746.../wsmsvol 07 no 02 paper 01pdf.

[14] Egbetade, S.A. and Ibrahim, M.O. (2012). Global stability results for a tuberculosis epidemic model. *Res. J. Math. & Stat*. 4(1), 14-20.

[15] Li, J. and Cui, N. (2013). Bifurcation and Chaotic Behaviour of a Discrete-Time SIS Model. *Discrete Dynamics in Nature and Society* 2013, 85-93.

[16] Gyasi-Agyei, K.A. Gyasi-Agyei, A. and Obeng-Denteh, W. (2014). Mathematical modeling of the epidemiology of Tuberculosis in the Ashanti Region of Ghana. *British Journal of Mathematical /Computer Science* 4(3), 375-393.

[17] Egbetade, S.A., Ibrahim, M.O. and Ejieji, C.N. (2013). On existence of a vaccination model of tuberculosis disease pandemic. *Int. J. Engrg. & Sc.* 2(7), 41-44.

[18] Diekmann, O. and Heesterbeek, J.A.P. (2000). Mathematical epidemiology of Infectious Disease. John Wiley & Sons, Chechester.

[19] Maplesoft 15 (2011). Waterloo Maple Inc., Ontario, Canada.