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GLOBAL ANALYSIS OF DISEASE-FREE EQUILIBRUM OF A MATHEMATICAL MODEL OF TUBERCULOSIS USING LYAPUNOV METHOD

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Abstract

A mathematical model for the dynamics of tuberculosis infection is studied in this paper. The global stability of disease-free equilibrium (DFE) is obtained by Lyapunor method and Lasalle Invariance principle. In addition we derive the basic reproduction (R_0). The result showed that the disease-free equilibrium is globally asymptotically stable if $R_0 < 1$ and the disease dies off. This suggests that to effectively control the spread and transmission of tuberculosis, the threshold parameter, R_0, must constantly lies below unity. Hence, medical practitioners and all TB stakeholders must focus on increasing treatment of infected individuals in order to reduce R_0, the parameter that determined whether or not the disease will spread through the population.

Keywords: Mathematical model, tuberculosis, disease-free equilibrium, basic reproduction number, treatment

1. Introduction

Tuberculosis (TB) is a contagious disease that affects all ages and kills nearly 5000 people every day worldwide [1]. Globally, it is a major public health concern because it is responsible for 1.2-1.5 million deaths with 85% of this occurring in developing countries and 26% in Africa [2]. Although, TB is currently well controlled as evident in the reduction of number of deaths in recent years, TB levels are increasing in Africa and Southern Asia [3].

In Nigeria, the burden of tuberculosis is high. The increased rate in poverty, over-crowding, malnutrition, lack of TB drugs, underfunding of TB programs and non-adherence to TB policies are factors contributing to TB spread in the country [4]. The WHO estimates showed an incidence rate to be 311 per 100,000 populations and prevalence rate of 546/100,000 populations [5]. These figures ranked Nigeria 3rd highest Tb-burden country in the world and number one in Africa. The report also reveals that there were over 80% of TB undetected cases which served as reservoir for TB transmission. The challenges in TB control in Nigeria have been worsened by TB/HIV co-infection. In particular, HIV accelerates the activation of TB, thus leading to high failure rate of treatment.

There are two forms of TB namely: Pulmonary TB in Adults and TB meningitis in children while adult pulmonary TB is an important public health problem [6]. The main route of TB transmission is by air droplets of infected persons when they cough, sing, sneeze or talk. TB symptoms include chest pain, fatigue (tiredness), weight loss, loss of appetite, night sweats and whooping cough [6].

Over the years, the study of TB dynamics among populations has been modeled by many researchers. For example, Blower et al. [7] used a 3-D SEI model of TB to simulate TB mortality data and showed different rates of disease progression. The authors also conducted global dynamics of the disease and observed disease-free and endemic states under certain conditions. Jung et al [8] applied optimal control theory to a two-strain TB model. They concluded that a low cost combination of treatment would be a very effective way for reducing latent and active resistant-strain TB cases.

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In [9], the authors presented a mathematical model of TB to show the significance of WHO Directly Observed Therapy, Shortcourse (DOTS) in reducing TB incidence in Nigeria. Guo and Li [10] employed LaSalle principle and a global Lyapunov function to investigate global dynamics of a model of TB incorporating latent and clinical (active) TB and treatment. Nainggolan et al [11] proposed a SVIR compartmental model to assess the impact of vaccination on the transmission dynamics of TB. Athitan and Ghosh [12] analysed a TB disease transmission SEIR model with case detection. Ainseba et al. in [1] examined the combine use of screening for detection and treatment of latently infected individuals as TB control strategy. Nkamba et al. [13], using the Lyapunov-LaSalle method, proved global stability of a Susceptible, Early latent, Late latent, Infectious (SVELI) model of TB. Egbetade et al. [14] studied a tuberculosis model with treatment. Mathematical analysis of the model reveals that to effectively control the disease the treatment rate must lie above a certain threshold.

In this study, we consider the TB disease transmission model proposed by Egbetade [15]. Our main goal is to conduct global stability of disease-free equilibrium of the model. LaSalle invariance principle and a suitable Lyapunov function shall be used for the analysis.

3. Mathematical Formulation

The model is [15]

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

$$\frac{dE}{dt} = (1-\rho)\beta IS - (\mu + v)E \tag{2}$$

$$\frac{dI}{dt} = d\rho\beta IS - (\mu + \mu_T + 1)I \tag{3}$$

$$\frac{dR}{dt} = SI - \beta IR - \mu R \tag{4}$$

where all the variables and parameters have their usual meanings in [15]

The model has two equilibrium points which are disease-free equilibrium (DFE) and endemic equilibrium (EE).

At the equilibrium points,

$$S' = E' = I' = R' = 0 \tag{5}$$

Hence, the following equations is solved for equilibrium points

$$(1-\gamma)\pi - \beta IS - \mu S = 0 \tag{6}$$

$$(1-\rho)\beta IS - (\mu + v)E = 0 \tag{7}$$

$$d\rho\beta IS - (\mu + \mu_T + s)I = 0 \tag{8}$$

$$SI - \beta IR - \mu R = 0 \tag{9}$$

In a DFE, the population is free from TB infection, consequently, E=I=0 and equations (6) and (9) become

$$(1-\gamma)\pi - \mu S = 0 \tag{10}$$

$$-\mu R = 0 \tag{11}$$

Then, solving (10) – (11), we obtain the DFE point

$$A_0 = (S_0, E_0, I_0, R_0) = \left(\frac{(1-\gamma)\pi}{\mu}, 0, 0, 0\right) \tag{12}$$

For the endemic equilibrium, there is an existence of infection when $I \neq 0$. To find the endemic equilibrium $A^* = (S^*, E^*, I^*, R^*)$, we equate equations (1) – (4) to zero and rewrite as follows:\

$$(1-\gamma)\pi - BI^*S^* - \mu S^* = 0 \tag{13}$$

$$(1-\rho)BI^*S^* - (\mu + v)E^* = 0 \tag{14}$$

$$d\rho BI^*S^* - (\mu + \mu_T + s)I^* = 0 \tag{15}$$

$$sI^* - BI^*R^* - \mu R^* = 0 \tag{16}$$

Solving equation (15), we have

$$S^* = \frac{\mu + \mu_T + s}{d\rho\beta} \tag{17}$$

Then, substituting equation (17) into equation (15) yields

$$I^* = \frac{(1-\gamma)\pi d\rho\beta - \mu(\mu + \mu_T + s) = 0}{\beta(\mu + \mu_T + s)} \tag{18}$$

Using equation (17) and (18) in equation (14), we obtain

$$E^* = \frac{(1-\rho)\left[(1-\gamma)\pi d\rho\beta - \mu(\mu+\mu_T+s)\right]}{\mu+v} \tag{19}$$

Finally, by substituting equation (18) into equation (16) then we get

$$R^* = \frac{1}{\beta}\left[\frac{(1-\gamma)\pi d\rho\beta - \mu(\mu+\mu_T+s)}{(1-\gamma)\pi d\rho\beta - 2\mu(\mu+\mu_T+s)}\right] \tag{20}$$

Thus, we have the endemic equilibrium $A^* = \left(S^*, E^*, I^*, R^*\right)$ as defined in equations (17)-(20)

In this paper, we shall conduct global stability of model in the following invariant region

$$J = \left\{(S,E,I,R) \in \Re_+^4 : S \geq 0, E \geq 0, I \geq 0, R \geq 0, S+E+I+R \leq \frac{(1-\gamma)\pi}{\mu}\right\} \tag{21}$$

From [14], the basic reproduction number of the TB model is obtained as

$$R_0 = \frac{d\beta\pi(1-\gamma)}{\mu(\mu+\mu_T+s)} \tag{22}$$

4. Global Stability of DFE

We state and prove the following theorem

Theorem 1:

If $R_0 < 1$, then the DFE A_0 of equations (1) – (4) is globally asymptotically stable (GAS) in the region *J* given by equation (4.21)/

Proof

The proof of this theorem is based on the approach of Shuai and van den Driessche [16] for global stability of equilibrium states of epidemic models.

The variable *S* does not appear in the 1st term of susceptible compartment. By dropping this term, equation (1) – (4) reduce to

$$\left.\begin{aligned}
\frac{dS}{dt} &= S' - \beta IS - \mu S \\
\frac{dR}{dt} &= (1-\rho)\beta IS - (\mu+v)E \\
\frac{dI}{dt} &= d\rho\beta IS - (\mu+\mu_T+s)I \\
\frac{dR}{dt} &= sI - \beta IR - \mu R
\end{aligned}\right\} \tag{23}$$

Equation (23) is then analyzed for global stability of the disease-free equilibrium.

Consider a Lyapunov function

$$L(S,E,I,R) = fS + gE + hI + iR \tag{24}$$

where *f*, *g*, *h* and *i* are all positive constants

Taking the derivatives of L in equation (24) and substituting equation (23), give

$$\frac{dL}{dt} = fS' + gE' + hI' + iR' \tag{25}$$

$$= f(-\beta IS - \mu S) + \left[g(1-\rho)\beta IS - (\mu+v)E\right] + h\left[d\rho\beta IS - (\mu+\mu_T+s)I\right] + i(sI - \beta IR - \mu R) \tag{26}$$

$$= f(\mu S) - (f\beta + g\beta + g\rho\beta + hd\rho\beta)IS - g(\mu+v)E - h\left[(\mu+\mu_T+s) - is\right] - i\beta IR - \mu R \tag{27}$$

$$= -(f\mu)S - (f\beta + g\beta + g\rho\beta + hd\rho\beta)IS - g(\mu-v)E - hR_0\left(\frac{d\beta\pi(1-\gamma)}{\mu} - \frac{1}{R_0}is\right)I - i\beta iR - i\mu R \tag{28}$$

Since the model described human population, $\mu > 0, \beta > 0, d > 0, v > 0, \rho > 0, \pi > 0, \gamma > 0$. It follows then that

$$\left.\begin{aligned}
&-f\mu < 0 \\
&-(f\beta - g\beta + g\rho\beta + hd\rho\beta) < 0 \\
&-g(\mu+v) < 0 \\
&-i\beta < 0 \\
&-i\mu < 0
\end{aligned}\right\} \tag{29}$$

Now, R_0<1 in (29) implies that

$$-hR_0\left(\frac{d\beta\pi(1-\gamma)}{\mu}-\frac{1}{R_0}is\right)<0$$

and in view of (29), it is evident that $\frac{dL}{dt}<0$ in J. Furthermore, $\frac{dL}{dt}<0$ only if S = E = I = R = 0. Hence, the maximum (largest) invariant set in $\left\{(S,E,I,R):\frac{dL}{dt}=0\right\}$ is the singleton $\{A_0\}$.By LaSalle's invariance principle [17], every solution of equations (1)- (4) with initial conditions in *J* tends to DFE A_0 as $t\to\infty$. Hence, the disease-free equilibrium A_0 is globally asymptotically stable in the invariant region J if $R_0<1$.

5. Discussion of Results and Conclusion

We have investigated the global dynamics of disease-free equilibrium of a TB epidemic model. Analytical result showed that the model is globally asymptotically stable if $R_0<1$. The interpretation of this result is that TB infection under this situation is temporal and will disappear in time.

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