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On Existence of a Vaccination Model of Tuberculosis Disease Pandemic

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Abstract: *In this paper, we propose a vaccine-dependent mathematical model for the treatment of tuberculosis epidemics at the population level. We formulate a theorem on existence and uniqueness of solution and establish the proof of the theorem. In addition, we show that the infection is cleared from the population if* $R_0 < 1$.

Keywords: *Tuberculosis; mathematical model; existence and uniqueness of solution; basic reproduction number; vaccine*

I. INTRODUCTION

Undoubtedly, Tuberculosis (TB) pandemic is one of the greatest public disasters of modern times. The global burden of tuberculosis has increased over the years despite widespread implementation of control measures including BCG vaccination and the WHO's DOTS strategy which focuses on case finding and short-course therapy [4, 10].According to the estimates of the World Health Organization (WHO), an estimated 13.7 million people acquired the disease in 2007 resulting in 1.8 million deaths mostly in developing countries [19]. Africa alone had 8.8 million new TB infections which results in 1.7 million deaths in 2003 [20]. Of all African countries, Nigeria has the highest TB burden and is ranked 4th among 22 high TB burden countries in the world [21]. Studies suggest that more people in the developed world would contract TB because their immune systems are more likely to be compromised due to higher exposure to immune suppressive drugs, substance abuse or AIDS [1, 11, 15]. Tuberculosis infection can be transmitted through primary progression after a recent infection, re-activation of a latent infection and re-infection of a previously infected individual [9]. A small proportion of those infected will develop primary disease within several years of their first infection. Those who escape primary disease may eventually re-activate this latent infection decades after an initial transmission event. Lastly, latently infected individual can be re-infected by a process known as exogenous re-infection and develop the disease as a result of this new exposure [7].

Despite some successes associated with the use of Bacilli Calmette-Guerin (BCG) vaccines and some TB treatment therapies, this pandemic has continued to increase and has led to a growing consensus that new control strategies will be needed for disease eradication. The rise in TB incidence has been attributed to the emergence of multi- drug-resistant TB strains, the spread of HIV, the collapse of public health programs and the deadly combination of HIV (human immune deficiency virus) and TB epidemics [2,4,8,9,13]. In more than half of all HIV – related deaths, tuberculosis is the "opportunistic infection" which takes advantage of an immune system already compromised by HIV [16]. Most of the current resurgence of the disease is in sub-Saharan Africa, Eastern Europe and Asia [11].Mathematical models have been used extensively to study the transmission dynamics of TB epidemics (see [3,5,6,7,9,10,14] and the references therein). The dynamics of these models tend to generally be completely determined by a threshold quantity called the basic reproduction number (denoted by R_0) which measures the number of new cases an index case can generate in a completely susceptible population [17]. In particular, when $R_0 < 1$, a small influx of infected individuals will not generate large outbreaks, the disease dies out in time and the epidemic-free equilibrium is asymptotically stable. On the other hand, infection will persist and an epidemic results if $R_0 > 1$ and a stable epidemic equilibrium exists. In the present paper, we propose a deterministic SVEIR vaccination model for tuberculosis at the population level. We show local asymptotic stability of the infection-free equilibrium when $R_0 < 1$.We formulate a theorem on existence and uniqueness of solution and establish the proof.

II. MATHEMATICAL FORMULATION

Individuals enter the population at a rate π. A proportion, n, of individuals entering the population are vaccinated and enter the vaccinated class V. We denote classes of suspectible by S, latently infected and unvaccinated by E, latently infected and vaccinated by E_v, actively infected by I and recovered by R.

Susceptible individuals once infected can either progress quickly to active TB at a rate ρ or develop a latent infection and move slowly to active TB at a rate v. Our model is thus given by

$$S' = (1-\gamma)(1-n)\pi + qV - \beta IS/N - \mu S \quad (1)$$

$$V' = n(1-\gamma)\pi - qV - (1-f_1)\beta VI/N - \mu V \quad (2)$$

$$E' = (1-\rho)\beta IS/N - (v+\mu+\varepsilon)E + \rho\beta IE/N \quad (3)$$

$$E_v' = (1-\rho)(1-f_1)(1-f_2)\beta IV/N - (\mu+v+\varepsilon)E \quad (4)$$

$$I' = dvE + \rho\beta IS/N + \rho(1-f_1)(1-f_2)\beta IV/N - (\mu+\mu_T+m)I \quad (5)$$

$$R' = smI + s\varepsilon E - \mu R - \beta IR/N \quad (6)$$

where $N = S + V + E + E_v + I + R$ is the total size of the population, k is the threshold for the benefit of vaccination and all other parameters are as defined below

q = rate at which the vaccine wanes

d = detection rate of active TB

s = treatment rate of active TB

μ = natural death rate

μ_T = death rate due to TB infection

m = clearance rate for TB induced death

γ = proportion of recruitment due to immigration

β = transmission rate

ε = rate at which susceptible individuals recover

f_1 = efficacy of vaccines in preventing initial progression

f_2 = efficacy of vaccines in preventing fast progression

Lemma: The basic reproduction number for our model system (1) – (6) is

$$R_0 = \frac{\rho\beta[\mu(1-n)+q]\pi}{\mu(\mu+q)(\mu+\rho)(\mu+\varepsilon)} \quad (7)$$

We consider the epidemic-free equilibrium state of our model and take parameter values in equations (1) – (6) as follows: $\rho = 0.004$, $n = 0.14$, $q = 0.37$, $\beta = 0.0238$, $\pi = 0.30$, $\mu = 0.01425$, $\varepsilon = 0.13$. We calculate the basic reproduction number as $R_0 = 0.75736$. This shows that the infection is temporal and can be eradicated in finite time.

III. EXISTENCE AND UNIQUENESS OF SOLUTION

We formulate theorem on existence of unique solution of model system (1) – (6) and we establish the proof. We consider the system of linear equations below

$$\left.\begin{aligned} x_1' &= f_1(t, x_1, \dots, x_n) \\ x_2' &= f_2(t, x_1, \dots, x_n) \\ &\vdots \\ x_n' &= f_n(t, x_1, \dots, x_n) \end{aligned}\right\} \quad (8)$$

We may write equation (8) in compact form as

$$x' = f(t,x), \qquad x(t_0) = x_0 \tag{9}$$

Theorem 1 [12]

Let D denote the region

$$|t - t_0| \leq a, \quad \| x - x_0 \| \leq b, \; x = (x_1, x_2, \dots, x_n), \; x_0 = (x_{10}, x_{20}, \dots, x_{n0}) \tag{10}$$

and suppose that $f(t,x)$ satisfies the Lipschitz condition

$$\| f(t,x_1) - f(t,x_2) \| \leq k \, \| x_1 - x_2 \| \tag{11}$$

whenever the pairs (t,x_1) and (t,x_2) belong to D, where k is a positive constant. Then, there is a constant $\delta > 0$ such that there exists a unique continuous vector solution $\underline{x}(t)$ of the system (9) in the interval $|t - t_0| \leq \delta$.

It is important to note that condition (11) is satisfied by the requirement that $\frac{\partial f_i}{\partial x_j}$, $i,j = 1,2,\dots,n$ are continuous and bounded in D.

We now return to our model equations (1) – (6). We are interested in the region

$$0 \leq \alpha \leq R \tag{12}$$

We look for a bounded solution in this region and whose partial derivatives satisfy $\delta \leq \alpha \leq 0$, where α and δ are positive constants.

We now use the theorem above to state our own theorem below:

Theorem 2

Let D' denote the region $0 \leq \alpha \leq R$. Then, equation (1) – (6) has a unique solution.

Proof

We show that $\frac{\partial f_i}{\partial x_j}$, $i,j = 1,2,3,4,5,6$ are continuous and bounded in D'.

Let

$$f_1 = (1-\gamma)(1-n)\pi + qV - \beta IS/N - \mu S \tag{13}$$

$$f_2 = n(1-\gamma)\pi - qV - (1-f_1)\,\beta VI/N - \mu V \tag{14}$$

$$f_3 = (1-\rho)\,\beta IS/N - (v+\mu+\varepsilon)E + \rho\beta IE/N \tag{15}$$

$$f_4 = (1-\rho)(1-f_1)(1-f_2)\,\beta IV/N - (\mu+v+\varepsilon)E \tag{16}$$

$$f_5 = dvE + \rho\beta IS/N + \rho(1-f_1)(1-f_2)\,\beta IV/N - (\mu+\mu_T+m)\,I \tag{17}$$

$$f_6 = smI + s\varepsilon E - \mu R - \beta IR/N \tag{18}$$

Using equation (13), we have the partial derivatives below

$$\left.\begin{aligned} \left|\frac{\partial f_1}{\partial S}\right| &= |-\beta I/N - \mu| < \infty \\ \left|\frac{\partial f_1}{\partial V}\right| &= |q| < \infty \\ \left|\frac{\partial f_1}{\partial E}\right| &= \left|\frac{\partial f_1}{\partial E_v}\right| = \left|\frac{\partial f_1}{\partial R}\right| = 0 < \infty \\ \left|\frac{\partial f_1}{\partial I}\right| &= |-\beta S/N| < \infty \end{aligned}\right\} \tag{19}$$

These partial derivatives exist, continuous and are bounded in the same way the other derivatives exist and are bounded. Hence, by Theorem 2, the model system (1) – (6) has a unique solution.

IV. DISCUSSION AND CONCLUSION

In this paper, we discussed a mathematical model of TB with a focus on vaccination for the treatment of active TB.We proved existence and uniqueness of solution in order to ascertain the existence of the model. The model proposed in this paper can used in interactive workshops with health planners and other stakeholders in TB control so that participants could gain a better understanding of how BCG vaccines could be used to control the disease. In addition, the model can be applied to specific-country data on TB and then simulated over a given time frame in order to estimate the number of new TB infections so that prevention and intervention strategies could be properly designed.

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