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SOLUTION OF AN INFECTION AGE-STRUCTURED MATHEMATICAL MODEL FOR TUBERCULOSIS DISEASE DYNAMICS USING THE HOMOTOPY PERTURBATION METHOD

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Abstract

The solution of an infection-age-structured mathematical model for tuberculosis (TB) disease dynamics using the homotopy perturbation method is presented. The proof of the existence and uniqueness of solution to the model equations were obtained and shown to be continuously dependent on the initial age-of-infection. The model was next solved the homotopy perturbation method. Results obtained from the analytical solution are simulated for the latent and infectious classes using Maple 17 mathematical software. The results reveal that treatment of TB is faster with the latent TB individuals than the actively infected individuals. This clearly implies that, treatment of TB is faster when the infection age of TB is low and slower when the infection age of TB is high.

***Keywords*:** Age-of-Infection, tuberculosis, homotopy perturbation method

1.0 Introduction

Tuberculosis otherwise known as *tubercle bacillus* (TB) remains one of the top 10 world's most infectious deadly killer disease. TB ranks as the second leading cause of death from an infectious disease worldwide after the human immunodeficiency virus (HIV), World Health Organization [1]. Over the years most epidemiological models are formulated using non-linear ordinary differential equations [2-5]. Few authors have formulated infection-age-structured models which most at times, gives rise to integro-differential equations (IDEs) [6-9].

Integro-differential equations have a great deal of application in different branches of sciences and engineering. It arises naturally in a variety of models from biological science, applied mathematics, ph\ysics and other disciplines, such as theory of elasticity, forecasting human population, population dynamics, fluid dynamics, oscillating magnetic field amongst others [8, 10]. Therefore, finding the analytical approximation of such equations are of great interest to mathematical epidemiologists and other scientists alike.

In this paper, the solution of the integro-differential equation for the infection-age-structured model is provided using the homotopy perturbation method.

2.0 Model Equations

The following model equations are formulated as in Ashezua [7].

$$\frac{dS(t)}{dt} = (1-\upsilon)\Lambda - \alpha(1-\theta)S(t)I(t) - \alpha\theta(1-\psi_e)S(t)I(t) + \omega V(t) + \phi T(t) - \mu S(t) \quad (1)$$

$$\frac{dV(t)}{dt} = \upsilon\Lambda - (\mu+\omega)V(t) \quad (2)$$

$$\frac{\partial l(t,\tau)}{\partial t} + \frac{\partial l(t,\tau)}{\partial \tau} + (\mu+\gamma+\rho_2)l(t,\tau) = 0 \quad (3)$$

$$\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} + (\mu+\delta+\rho_1)i(t,\tau) = 0 \quad (4)$$

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$$\frac{dT(t)}{dt} = \rho_2 L(t) + \rho_1 I(t) - (\mu + \phi)T(t) \tag{5}$$

$$l(t,0) = B_1(t) = \alpha(1-\theta)S(t)I(t) \tag{6}$$

$$i(t,0) = B_2(t) = \alpha\theta(1-\psi_e)S(t)I(t) + \gamma L(t) \tag{7}$$

The total population size is given by

$$N(t) = S(t) + V(t) + L(t) + I(t) + T(t), \tag{8}$$

where

$$L(t) = \int_0^T l(t,\tau)d\tau \tag{9}$$

$$I(t) = \int_0^T i(t,\tau)d\tau \tag{10}$$

$$S(0) = S_0,\ V(0) = V_0,\ L(0) = L_0,\ I(0) = I_0,\ N(0) = N_0 \tag{11}$$

$$l(0,\tau) = \phi_1(\tau) \tag{12}$$

$$i(0,\tau) = \phi_2(\tau) \tag{13}$$

3.0 Methods of Solution

3.1 Existence and Uniqueness of Solution

In this section, the criterion for the existence and uniqueness of solution of problem (3) and (4) is established following a similar approach as in Ashezua [6]. Solving equations (3) and (4) along the characteristics lines yields:

$$l(t,\tau) = \begin{cases} B_1(t-\tau)\pi_1(\tau), t > \tau \\ \phi_1(\tau - t)\pi_1(\tau), t < \tau \end{cases}, \tag{14}$$

where

$$\pi_1(\tau) = e^{-(\mu + \gamma + \rho_2)\tau} \tag{15}$$

and

$$i(t,\tau) = \begin{cases} B_2(t-\tau)\pi_2(\tau), t > \tau \\ \phi_2(\tau - t)\pi_2(\tau), t < \tau \end{cases}, \tag{16}$$

where

$$\pi_2(\tau) = e^{-(\mu + \delta + \rho_2)\tau} \tag{17}$$

The proof of the existence and uniqueness of solution for the model equations (1), (2) and (5) are similar to the one found in the works of Egbetade *et al.* [3].

3.2 Solution of the Model

3.2.1 Homotopy Perturbation Method (HPM)

To illustrate the basic ideas of this method, the following non-linear differential equation is considered as outlined in the works of He [11]:

$$A(u) - f(r) = 0, \qquad r \in \Omega, \tag{18}$$

Subject to the boundary condition

$$B\left(u, \frac{\partial u}{\partial n}\right) = 0, \qquad r \in \Gamma \tag{19}$$

Where A is a general differential operator, B is a boundary operator, $f(r)$ a known analytical function and Γ is the boundary of the domain Ω. . The operator A can be divided into two parts of L and N, where L is the linear part, while N is a non-linear one.

$$L(u)+N(u)-f(r)=0, \qquad r\in\Omega, \tag{20}$$

Using the Homotopy technique, we construct a Homotopy $v(r,p):\Omega\times[0,1]\to R$, which satisfies

$$H(v,p)=(1-p)[L(v)-L(u_0)]+p[L(v)+N(v)-f(r)]=0 \tag{21}$$

$$p\in[0,1],\quad r\in\Omega \tag{22}$$

or

$$H(v,p)=L(v)-L(u_0)+pL(u_0)+p[N(v)-f(r)]=0 \tag{23}$$

where ,

$L(u)$ is the linear part which is given by

$L(u)=L(v)-L(u_0)+pL(u_0)$

and $N(u)$ is the non-linear part

$N(u)=pN(v)$

In equation (21) $p\in[0,1]$ is an embedding parameter and u_0 is an initial approximation of (18) that satisfied the boundary condition. Obviously, considering equation (22) and (23), we have:

$$H(v,0)=L(v)-L(u_0)=0 \tag{24}$$

$$H(v,1)=L(v)+N(v)-f(r)=0 \tag{25}$$

The changing process of p from zero to unity is just of $H(v,r)$ from $u_0(r)$ to $u(r)$. In topology, this is called deformation and $L(v)-L(u_0)$ and $A(v)-f(r)$ are called homotopy.

According to HPM, we can first use the embedding parameter p as a small parameter

and assume that the solution of equation (22) and (23) can be written as power series in p :

$$v=v_0+pv_1+p^2v_2+\ldots \tag{26}$$

Setting $p=1$result in the approximate solution of (18) is:

$$u=\lim_{p\to1} v=v_0+v_1+v_2+\ldots \tag{27}$$

The series (27) is convergent for most cases. However, the convergence rate depends on the non-linear operator $A(v)$. The following observations are made by He [12]:

(i) The derivatives of $N(v)$ with respect to *v* must be small because the parameter p may be large, i.e. $p\to1$.

(ii) The norm of $L^{-1}\dfrac{\partial N}{\partial V}$ must be smaller than one so that the series converges.

Before applying the Homotpy perturbation method as used by He [11], equations (3) and (4) are solved using the chain rule as follows:

Solving equations (3) and (4) using the chain rule by letting $z=\tau+t$ and $t=z-\tau$ gives

$$l(t,\tau)=e^{k_1\tau-\frac{1}{2}[\mu+\gamma+\rho_2]t}, \tag{28}$$

and

$$i(t,\tau)=e^{k_2\tau-\frac{1}{2}[\mu+\delta+\rho_1]t}, \tag{29}$$

Substituting (28) and (29) into (9) and (10) and integrating with respect to τ respectively gives:

$$L(t) = \frac{\left\{\exp\left[\left(\mu+\delta+\rho_2\right)T - \frac{1}{2}\left(\mu+\delta+\rho_2\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_2\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_2\right)} \qquad (30)$$

and

$$I(t) = \frac{\left\{\exp\left[\left(\mu+\delta+\rho_1\right)T - \frac{1}{2}\left(\mu+\delta+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_1\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_1\right)} \qquad (31)$$

We next solve equations (1), (2) and (5) using the homotopy perturbation method.
Suppose the solution of $S(t), V(t)$ and $T(t)$ in (1), (2) and (5) can be expressed as:

$$S = x_0 + px_1 + p^2x_2 + \ldots \qquad (32)$$

$$V = y_0 + py_1 + p^2y_2 + \ldots \qquad (33)$$

$$T = z_0 + pz_1 + p^2z_2 + \ldots \qquad (34)$$

Applying homotopy to (1), (2) and (5) gives

$$(1-p)\frac{dS}{dt} + p\left[\frac{dS}{dt} - (1-\upsilon)\Lambda + \alpha(1-\theta)SI + \alpha\theta(1-\psi_e)SI - \omega V - \phi T + \mu S\right] = 0 \qquad (35)$$

$$(1-p)\frac{dV}{dt} + p\left[\frac{dV}{dt} - \upsilon\Lambda + (\mu+\omega)V\right] = 0 \qquad (36)$$

$$(1-p)\frac{dT}{dt} + \left[\frac{dT}{dt} - \rho_2 L - \rho_1 I + (\mu+\phi)T\right] = 0 \qquad (37)$$

Substituting (32), (33) and (34) into (35) simplifying and collecting coefficients of the powers of p gives

$$p^0 : x_0' = 0 \qquad (38)$$

$$p^1 : x_1' - \phi z_0 - \omega y_0 - (1-\upsilon)\Lambda + \frac{\alpha(1-\theta)x_0\left\{\exp\left[\left(\mu+\delta+\rho_1\right)T - \frac{1}{2}\left(\mu+\delta+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_1\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_1\right)}$$
$$+ \frac{\alpha\theta\left(1-\psi_e\right)x_0\left\{\exp\left[\left(\mu+\delta+\rho_1\right)T - \frac{1}{2}\left(\mu+\delta+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_1\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_1\right)} + \mu x_0 = 0 \qquad (39)$$

$$p^2 : x_2' - \phi z_1 + \frac{\alpha(1-\theta)x_1\left\{\exp\left[\left(\mu+\delta+\rho_1\right)T - \frac{1}{2}\left(\mu+\delta+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_1\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_1\right)} - \omega y_1$$
$$+ \frac{\alpha\theta\left(1-\psi_e\right)x_1\left\{\exp\left[\left(\mu+\delta+\rho_1\right)T - \frac{1}{2}\left(\mu+\delta+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\delta+\rho_1\right)t\right)\right)\right\}}{\left(\mu+\delta+\rho_1\right)} + \mu x_1 = 0 \qquad (40)$$

Substituting (33) into (36), expanding and collecting coefficients of the powers of p gives

$$p^0 : y_0' = 0 \qquad (41)$$

$$p^1 : y_1' - \upsilon\Lambda + (\mu+\omega)y_0 = 0 \qquad (42)$$

$$p^2 : y_2' + (\mu+\omega)y_1 = 0 \qquad (43)$$

Substituting (34) into (37), expanding and collecting the coefficients of the powers of p gives:

$$p^0 : z_0' = 0 \qquad (44)$$

$$p^1 : z_1^{'} + (\mu+\phi)z_0 - \frac{\rho_2\left\{\exp\left[\left(\mu+\gamma+\rho_2\right)t - \frac{1}{2}\left(\mu+\gamma+\rho_2\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\gamma+\rho_2\right)t\right)\right)\right\}}{(\mu+\gamma+\rho_2)}$$

$$-\frac{\rho_1\left\{\exp\left[\left(\mu+\gamma+\rho_1\right)t - \frac{1}{2}\left(\mu+\gamma+\rho_1\right)t\right] - \exp\left(-\frac{1}{2}\left(\left(\mu+\gamma+\rho_1\right)t\right)\right)\right\}}{(\mu+\gamma+\rho_1)} = 0 \quad (45)$$

$$p^2 : z_2^{'} + (\mu+\phi)z_1 \quad (46)$$

Solving (38), (41) and (44) gives

$$x_0 = S_0 \quad (47)$$

$$y_0 = V_0 \quad (48)$$

$$z_0 = T_0 \quad (49)$$

Substituting (32), (33) and (34) into (39), (42) and (45) respectively and solving yields (50), (52) and (53)

$$x_1 = \phi T_0 t + \omega V_0 t + (1-\upsilon)\Lambda t - \mu S_0 t - \frac{\alpha(1-\theta)S_0\left(\frac{e^{AT-\frac{1}{2}At}}{-\frac{1}{2}A} + \frac{e^{-\frac{1}{2}At}}{\frac{1}{2}A}\right)}{A}$$

$$-\frac{\alpha\theta(1-\psi_e)S_0\left(\frac{e^{AT-\frac{1}{2}At}}{-\frac{1}{2}A} + \frac{e^{-\frac{1}{2}At}}{\frac{1}{2}A}\right)}{A} \quad (50)$$

where

$$A = \mu+\delta+\rho_1 \quad (51)$$

$$y_1 = [\upsilon\Lambda - (\mu+\omega)V_0]t \quad (52)$$

$$z_1 = \frac{\rho_2\left(\frac{e^{\frac{1}{2}Bt}}{\frac{1}{2}B} + \frac{e^{-\frac{1}{2}Bt}}{\frac{1}{2}B}\right)}{B} + \frac{\rho_1\left(\frac{e^{\frac{1}{2}Ct}}{\frac{1}{2}Ct} + \frac{e^{-\frac{1}{2}Ct}}{\frac{1}{2}C}\right)}{C} - (\mu+\phi)T_0 t \quad (53)$$

where

$$B = \mu+\gamma+\rho_2 \quad (54)$$

$$C = \mu+\gamma+\rho_1 \quad (55)$$

Substituting (50) and (53) into (40) yields

$$x_2 = \int\left[\phi z_1 - \frac{\alpha(1-\theta)x_1\left(\left(e^{AT-\frac{1}{2}At}\right) - e^{-\frac{1}{2}At}\right)}{A} + \omega y_1 - \frac{\alpha\theta(1-\psi_e)x_1\left(\left(e^{AT-\frac{1}{2}At}\right) - e^{-\frac{1}{2}At}\right)}{A} - \mu x_1\right]dt \quad (56)$$

Substituting (52) into (43) gives

$$y_2 = -\int[(\mu+\omega)y_1]dt \quad (57)$$

Substituting (52) into (46) gives

$$z_2 = -\int[(\mu+\phi)z_1]dt \quad (58)$$

Substituting values of (47), (50) and (56) into (32) gives the analytical approximation for S. Also, substituting (48), (52) and (57) into (33) respectively gives the analytical approximation for V. Similarly, substituting (49), (53) and (58) into (34) gives the analytical approximation for T. The results from (30) and (31), that is the latent and actively infected compartments will be implemented in order to ascertain the behavior of the TB drugs in the body of both the latent and actively infected individuals as captured in section below.

4.0 Results and Discussion

The variables and parameters on Tables 1 and 2 are estimated following a similar approach as in the works of Ashezua [6].

Table 1: Values for population-dependent parameters of the model

S/NO	Variable/Parameter	Value	Source
1	S	36,368,808	WHO [1]
2	V	44,961,946	WHO [1]
3	L	73,197,680	WHO [1]
4	I	8,133,076	WHO [1]
5	T	51,366,792	WHO [1]
6	N	214,028,302	CIA [13]
7	μ	0.0181 yr^{-1}	CIA [13]
8	Λ	3,873,912	CIA [13]

Table 2: Values for population-independent parameters of the model

S/NO	**Parameter**	**Value**	**Source**
1	α	0.0000722 yr^{-1}	WHO [1]
2	ω	0.067 yr^{-1}	WHO [1]
3	γ	0.5 yr^{-1}	Assumed
4	θ	0.1 yr^{-1}	WHO [1]
5	$\rho_1, \ \rho_2, \tau, \upsilon, \psi_e$	(0-1) yr^{-1}	Assumed

Tables 1 and 2 were used to generate the plots on Figures 1 and 2 below respectively.

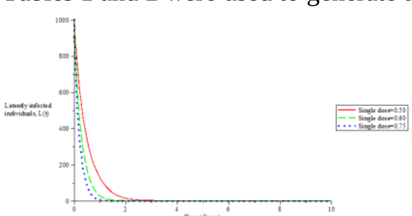

Figure 1: Latently infected individuals against time, t. Parameter values are as shown on Tables 1 and 2.

Figure 1 which is generated with the aid of Maple 17 from (30) shows a comparison when a single dose of isoniazid is administered when it is low, moderate and high as it affects the latently infected individuals. The above graphical profiles on Figure 1 shows that as the dosage administered to the latently infected individuals increases, the faster the recovery rate of the latently infected individuals with latent TB. It is however observed that when the efficacy of the dosage is at 75%, the latently infected individuals recover in about a years' time as compared to when the dosage is 50% and 60% respectively. This scenario is simulated for patients assumed to have latent TB infection.

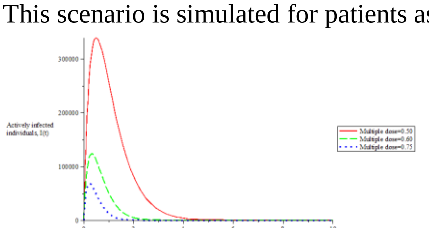

Figure 2: Actively infected individuals against time, t. Parameter values are as shown on Tables 1 and 2 respectively.

Figure 2 which is generated with the aid of Maple 17 from (31) shows comparison between 50%, 60% and 75% of the multiple dosages administered to the actively infected individuals with TB. It was observed that when the dosage is administered at 75% level, the individuals infected with TB actively are cured of the disease in more than a years' time (almost two years as shown on Figure 2). This result agrees with reality in the sense that, when patients take a full dosage of TB drugs, such a patient recover from the disease within a record time.

5.0 Conclusion

In this research work, the homotopy perturbation method was successfully applied to an infection-age-structured mathematical model for tuberculosis disease dynamics. Solutions were obtained for both the latent and infectious classes. Thereafter, analytical simulations of the results obtained were plotted using Maple 17 mathematical software. Results from the plots reveal that treatment of TB is faster with the latent TB individuals than the actively infected individuals. This clearly implies that, treatment of TB is faster when the infection age of TB is low and slower when the infection age of TB is high.

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